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(71) Applicant (for all designated States except US): ASTRA AKTIEBOLAG [SE/SE]; S-151 85 Södertälje (SE).

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(72) Inventors; and

08/891,928

- (75) Inventors/Applicants (for US only): SMITH, Douglas [US/US]; 2 Mayflower Lane, Gloucester, MA 01930 (US). ALM, Richard, A. [AU/US]; 28 Russet Hill Road, Ashland, MA 01721 (US).
- (74) Agents: MANDRAGOURAS, Amy, E. et al.; Lahive & Cockfiel, LLP, 28 State Street, Boston, MA 02109 (US).

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(54) Title: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO HELICOBACTER PYLORI AND VACCINE COMPO-SITIONS THEREOF

(57) Abstract

Recombinant or substantially pure preparations of H. pylori polypeptides are described. The nucleic acids encoding the polypeptides also are described. The H. pylori polypeptides are useful for diagnostics and vaccine compositions.

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NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO HELICOBACTER PYLORI AND VACCINE COMPOSITIONS THEREOF

Background of the Invention

Helicobacter pylori is a gram-negative, S-shaped, microaerophilic bacterium that was discovered and cultured from a human gastric biopsy specimen. (Warren, J.R. and B. Marshall, (1983) Lancet 1: 1273-1275; and Marshall et al., (1984) Microbios Lett. 25: 83-88). H. pylori has been strongly linked to chronic gastritis and duodenal ulcer disease. (Rathbone et. al., (1986) Gut 27: 635-641). Moreover, evidence is accumulating for an etiologic role of H. pylori in nonulcer dyspepsia, gastric ulcer disease, and gastric adenocarcinoma. (Blaser M. J., (1993) Trends Microbiol. 1: 255-260). Transmission of the bacteria occurs via the oral route, and the risk of infection increases with age. (Taylor, D.N. and M. J. Blaser, (1991) Epidemiol. Rev 13: 42-50). H. pylori colonizes the human gastric mucosa, establishing an infection that usually persists for decades. Infection by H. pylori is prevalent worldwide. Developed countries have infection rates over 50% of the adult population, while developing countries have infection rates reaching 90% of the adults over the age of 20. (Hopkins R. J. and J. G. Morris (1994) Am. J. Med. 97: 265-277).

The bacterial factors necessary for colonization of the gastric environment, and for virulence of this pathogen, are poorly understood. Examples of the putative virulence factors include the following: urease, an enzyme that may play a role in neutralizing gastric acid pH (Eaton et al., (1991) Infect. Immunol. 59: 2470-2475; Ferrero, R.L. and A. Lee (1991) Microb. Ecol. Hlth. Dis. 4: 121-134; Labigne et al., (1991) J. Bacteriol. 173: 1920-1931); the bacterial flagellar proteins responsible for motility across the mucous layer. (Hazell et al., (1986) J. Inf. Dis. 153: 658-663; Leying et al., (1992) Mol. Microbiol. 6: 2863-2874; and Haas et al., (1993) Mol. Microbiol. 8: 753-760); Vac A, a bacterial toxin that induces the formation of intracellular vacuoles in epithelial cells (Schmitt, W. and R. Haas, (1994) Molecular Microbiol. 12(2): 307-319); and several gastric tissue-specific adhesins. (Boren et al., (1993) Science 262: 1892-1895; Evans et al., (1993) J. Bacteriol. 175: 674-683; and Falk et al., (1993) Proc. Natl. Acad. Sci. USA 90: 2035-203).

Numerous therapeutic agents are currently available that eradicate *H. pylori* infections *in vitro*. (Huesca et. al., (1993) *Zbl. Bakt.* 280: 244-252; Hopkins, R. J. and J. G. Morris, supra). However, many of these treatments are suboptimally effective *in vivo* because of bacterial resistance, altered drug distribution, patient non-compliance or poor drug availabilty. (Hopkins, R. J. and J. G. Morris, supra). Treatment with antibiotics combined with bismuth are part of the standard regime used to treat *H. pylori* infection.

(Malfertheiner, P. and J. E. Dominguez-Munoz (1993) Clinical Therapeutics 15 Supp. B: 37-48). Recently, combinations of a proton pump inhibitors and a single antibiotic have been shown to ameliorate duodenal ulcer disease. (Malfertheiner, P. and J. E. Dominguez-Munoz supra). However, methods employing antibiotic agents can have the problem of the emergence of bacterial strains which are resistant to these agents. (Hopkins, R. J. and J. G. Morris, supra). These limitations demonstrate that new more effective methods are needed to combat *H. pylori* infections *in vivo*. In particular, the design of new vaccines that may prevent infection by this bacterium is highly desirable.

10 Summary of the Invention

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This invention relates to novel genes, e.g., genes encoding polypeptides such as bacterial surface proteins, from the organism *Helicobacter pylori* (*H. pylori*), and other related genes, their products, and uses thereof. The nucleic acids and peptides of the present invention have utility for diagnostic and therapeutics for *H. pylori* and other *Helicobacter* species. They can also be used to detect the presence of *H. pylori* and other *Helicobacter* species in a sample; and for use in screening compounds for the ability to interfere with the *H. pylori* life cycle or to inhibit *H. pylori* infection. More specifically, this invention features compositions of nucleic acids corresponding to entire coding sequences of *H. pylori* proteins, including surface or secreted proteins or parts thereof, nucleic acids capable of binding mRNA from *H. pylori* proteins to block protein translation, and methods for producing *H. pylori* proteins or parts thereof using peptide synthesis and recombinant DNA techniques. This invention also features antibodies and nucleic acids useful as probes to detect *H. pylori* infection. In addition, vaccine compositions and methods for the protection or treatment of infection by *H. pylori* are within the scope of this invention.

Detailed Description of the Drawings

Figure 1 is a bar graph that depicts the antibody titer in serum of mice following immunization with specific *H. pylori* antigens.

Figure 2 is a bar graph that depicts the antibody titer in mucous of mice following immunization with specific *H. pylori* antigens.

Figure 3 is a bar graph that depicts therapeutic immunization of *H. pylori* infected mice with specific antigens dissolved in HEPES buffer.

Figure 4 is a bar graph that depicts therapeutic immunization of *H. pylori* infected mice with specific antigens dissolved in buffer containing DOC.

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Figure 5 depicts the amino acid sequence alignment in a portion of the sequence of five *H. pylori* proteins (depicted in the single letter amino acid code; shown N-terminal to C-terminal, left to right).

Figure 6 depicts the amino acid sequence alignment in a portion of the sequence of four *H. pylori* proteins (depicted in the single letter amino acid code; shown N-terminal to C-terminal, left to right).

Figure 7 depicts the amino acid sequence alignment in a portion of the sequence of two *H. pylori* proteins (depicted in the single letter amino acid code; shown N-terminal to C-terminal, left to right).

Figure 8 depicts the amino acid sequence alignment in a portion of the sequence of two *H. pylori* proteins (depicted in the single letter amino acid code; shown N-terminal to C-terminal, left to right).

Detailed Description of the Invention

In one aspect, the invention features a recombinant or substantially pure preparation of *H. pylori* polypeptide of SEQ ID NO: 74. The invention also includes substantially pure nucleic acid encoding an *H. pylori* polypeptide of SEQ ID NO: 74, such nucleic acid is contained in SEQ ID NO: 1. The *H. pylori* polypeptide sequences of the invention described herein are contained in the Sequence Listing, and the nucleic acids encoding *H. pylori* polypeptides of the invention are contained in the Sequence Listing.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 75, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 2.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 76, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 3.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 77, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 4.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 78, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 5.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 79, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 6.

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In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 80, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 7.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 81, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 8.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 82, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 9.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 83, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 10.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 84, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 11.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 85, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 12.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 86, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 13.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 87, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 14.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 88, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 15.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 89, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 16.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 90, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 17.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 91, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 18.

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In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 92, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 19.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 93, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 20.

In another aspect, the invention features a substantially pure nucleic acid éncoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 94, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 21.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 95, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 22.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 96, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 23.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 97, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 24.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 98, such as a nucleic acid comprising a nucleotide sequence of SEO ID NO: 25.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 99, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 26.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 100, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 27.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 101, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 28.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 102, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 29.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 103, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 30.

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In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 104, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 31.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 105, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 32.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 106, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 33.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 107, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 34.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 108, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 35.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 109, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 36.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 110, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 37.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 111, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 38.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 112, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 39.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 113, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 40.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 114, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 41.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 115, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 42.

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In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 116, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO:43.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 117, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 44.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 118, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 45.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 119, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 46.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 120, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 47.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 121, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 48.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 122, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 49.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 123, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 50.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 124, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 51.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 125, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 52.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 126, such as a nucleic acid comprising a nucleotide sequence of SEO ID NO: 53.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 127, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 54.

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In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 128, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 55.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 129, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 56.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 130, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 57.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 131, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 58.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 132, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 59.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 133, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 60.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 134, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 61.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 135, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 62.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 136, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 63.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 137, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 64.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 138, such as a nucleic acid comprising a nucleotide sequence of SEO ID NO: 65.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 139, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 66.

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In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 140, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 67.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 141, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 68.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 142, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 69.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 143, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 70.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 144, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 71.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 145, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 72.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 146, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 73.

Particularly perferred is an isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cell envelope polypeptide or a fragment thereof. Such nucleic acid is selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, SEQ ID NO: 48, SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, SEQ ID NO: 71, SEQ ID NO: 17, SEQ ID NO: 57, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 8, and SEQ ID NO: 21.

In another embodiment, the *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof encoded by the nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, and SEQ ID NO: 48.

In another embodiment, the *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof encoded by the nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 10,

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SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, and SEQ ID NO: 71.

In another embodiment, the *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof encoded by the nucleic acid selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, and SEQ ID NO:71.

In yet another embodiment, the *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof encoded by the nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, and SEQ ID NO: 58.

Particularly preferred is an isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* secreted polypeptide or a fragment thereof. Such nucleic acid is selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 32, SEQ ID NO: 51, SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 22, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 53, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, and SEQ ID NO: 68.

Particularly preferred is an isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cellular polypeptide or a fragment thereof. Such nucleic acid is selected from the group consisting of SEQ ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 47, SEQ ID NO: 50, SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 69, SEQ ID NO: 70, and SEQ ID NO: 73.

Particularly preferred is a purified or isolated *H. pylori* cell envelope polypeptide or a fragment thereof, wherein the polypeptide is selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, SEQ ID NO: 121, SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID

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NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, SEQ ID NO: 130, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, and SEQ ID NO: 94.

In another embodiment, the *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, and SEQ ID NO: 121.

In another embodiment, the *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, and SEQ ID NO: 130.

In another embodiment, the *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof selected from the group consisting of SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, and SEQ ID NO:144.

In another embodiment. the *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131.

Particularly preferred is a purified or isolated *H. pylori* secreted polypeptide or a fragment thereof, wherein the polypeptide is selected from the group consisting of SEQ ID NO: 145, SEQ ID NO: 105, SEQ ID NO: 124, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 82, SEQ ID NO: 86, SEQ ID NO: 95, SEQ ID NO: 102, SEQ ID NO: 104, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 122, SEQ ID NO: 126, SEQ ID NO: 132, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, and SEQ ID NO: 141.

Particularly preferred is a purified or isolated *H. pylori* cellular polypeptide or a fragment thereof, wherein the polypeptide is selected from the group consisting of SEQ ID NO: 85, SEQ ID NO: 88, SEQ ID NO: 93, SEQ ID NO: 96, SEQ ID NO: 97, SEQ

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ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 120, SEQ ID NO: 123, SEQ ID NO: 133, SEQ ID NO: 137, SEQ ID NO: 142, SEQ ID NO: 143, and SEQ ID NO: 146.

In another aspect, the invention pertains to any individual *H. pylori* polypeptide member or nucleic acid encoding such a member from the above-identified groups of *H. pylori* polypeptides.

In another aspect, the invention features nucleic acids capable of binding mRNA of *H. pylori*. Such nucleic acid is capable of acting as antisense nucleic acid to control the translation of mRNA of *H. pylori*. A further aspect features a nucleic acid which is capable of binding specifically to an *H. pylori* nucleic acid. These nucleic acids are also referred to herein as complements and have utility as probes and as capture reagents.

In another aspect, the invention features an expression system comprising an open reading frame corresponding to *H. pylori* nucleic acid. The nucleic acid further comprises a control sequence compatible with an intended host. The expression system is useful for making polypeptides corresponding to *H. pylori* nucleic acid.

In another aspect, the invention features a cell transformed with the expression system to produce *H. pylori* polypeptides.

In another aspect, the invention features a method of generating antibodies against *H. pylori* polypeptides which are capable of binding specifically to *H. pylori* polypeptides. Such antibodies have utility as reagents for immunoassays to evaluate the abundance and distribution of *H. pylori*-specific antigens.

In another aspect, the invention features a method of generating vaccines for immunizing an individual against *H. pylori*. The vaccination method includes: immunizing a subject with at least one *H. pylori* polypeptide according to the present invention, e.g., a surface or secreted polypeptide, or active portion thereof, and a pharmaceutically acceptable carrier. Such vaccines have therapeutic and/or prophylactic utilities.

In another aspect, the invention provides a method for generating a vaccine comprising a modified immunogenic *H. pylori* polypeptide, e.g., a surface or secreted polypeptide, or active portion thereof, and a pharmacologically acceptable carrier.

In another aspect, the invention features a method of evaluating a compound, e.g. a polypeptide, e.g., a fragment of a host cell polypeptide, for the ability to bind an *H. pylori* polypeptide. The method includes: contacting the candidate compound with an *H. pylori* polypeptide and determining if the compound binds or otherwise interacts with an *H. pylori* polypeptide. Compounds which bind *H. pylori* are candidates as activators or inhibitors of the bacterial life cycle. These assays can be performed *in vitro* or *in vivo*.

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In another aspect, the invention features a method of evaluating a compound, e.g. a polypeptide, e.g., a fragment of a host cell polypeptide, for the ability to bind an *H. pylori* nucleic acid, e.g., DNA or RNA. The method includes: contacting the candidate compound with an *H. pylori* nucleic acid and determining if the compound binds or otherwise interacts with an *H. pylori* polypeptide. Compounds which bind *H. pylori* are candidates as activators or inhibitors of the bacterial life cycle. These assays can be performed *in vitro* or *in vivo*.

The invention features H. pylori polypeptides, preferably a substantially pure preparation of an H. pylori polypeptide, or a recombinant H. pylori polypeptide. In preferred embodiments: the polypeptide has biological activity; the polypeptide has an amino acid sequence at least 60%, 70%, 80%, 90%, 95%, 98%, or 99% identical or homologous to an amino acid sequence of the invention contained in the Sequence Listing, preferably it has about 65% sequence identity with an amino acid sequence of the invention contained in the Sequence Listing, and most preferably it has about 92% to about 99% sequence identity with an amino acid sequence of the invention contained in the Sequence Listing; the polypeptide has an amino acid sequence essentially the same as an amino acid sequence of the invention contained in the Sequence Listing; the polypeptide is at least 5, 10, 20, 50, 100, or 150 amino acid residues in length; the polypeptide includes at least 5, preferably at least 10, more preferably at least 20, more preferably at least 50, 100, or 150 contiguous amino acid residues of the invention contained in the Sequence Listing. In yet another preferred embodiment, the amino acid sequence which differs in sequence identity by about 7% to about 8% from the H. pylori amino acid sequences of the invention contained in the Sequence Listing is also encompassed by the invention.

In preferred embodiments: the *H. pylori* polypeptide is encoded by a nucleic acid of the invention contained in the Sequence Listing, or by a nucleic acid having at least 60%, 70%, 80%, 90%, 95%, 98%, or 99% homology with a nucleic acid of the invention contained in the Sequence Listing.

In a preferred embodiment, the subject *H. pylori* polypeptide differs in amino acid sequence at 1, 2, 3, 5, 10 or more residues from a sequence of the invention contained in the Sequence Listing. The differences, however, are such that the *H. pylori* polypeptide exhibits an *H. pylori* biological activity, e.g., the *H. pylori* polypeptide retains a biological activity of a naturally occurring *H. pylori* polypeptide.

In preferred embodiments, the polypeptide includes all or a fragment of an amino acid sequence of the invention contained in the Sequence Listing; fused, in reading frame, to additional amino acid residues, preferably to residues encoded by genomic

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DNA 5' or 3' to the genomic DNA which encodes a sequence of the invention contained in the Sequence Listing.

In yet other preferred embodiments, the *H. pylori* polypeptide is a recombinant fusion protein having a first *H. pylori* polypeptide portion and a second polypeptide portion, e.g., a second polypeptide portion having an amino acid sequence unrelated to *H. pylori*. The second polypeptide portion can be, e.g., any of glutathione-S-transferase, a DNA binding domain, or a polymerase activating domain. In preferred embodiment the fusion protein can be used in a two-hybrid assay.

Polypeptides of the invention include those which arise as a result of alternative transcription events, alternative RNA splicing events, and alternative translational and postranslational events.

The invention also encompasses an immunogenic component which includes at least one *H. pylori* polypeptide in an immunogenic preparation; the immunogenic component being capable of eliciting an immune response specific for the *H. pylori* polypeptide, e.g., a humoral response, an antibody response, or a cellular response. In preferred embodiments, the immunogenic component comprises at least one antigenic determinant from a polypeptide of the invention contained in the Sequence Listing.

In another aspect, the invention provides a substantially pure nucleic acid having a nucleotide sequence which encodes an *H. pylori* polypeptide. In preferred embodiments: the encoded polypeptide has biological activity; the encoded polypeptide has an amino acid sequence at least 60%, 70%, 80%, 90%, 95%, 98%, or 99% homologous to an amino acid sequence of the invention contained in the Sequence Listing; the encoded polypeptide has an amino acid sequence essentially the same as an amino acid sequence of the invention contained in the Sequence Listing; the encoded polypeptide is at least 5, 10, 20, 50, 100, or 150 amino acids in length; the encoded polypeptide comprises at least 5, preferably at least 10, more preferably at least 20, more preferably at least 50, 100, or 150 contiguous amino acids of the invention contained in the Sequence Listing.

In preferred embodiments: the nucleic acid of the invention is that contained in the Sequence Listing; the nucleic acid is at least 60%, 70%, 80%, 90%, 95%, 98%, or 99% homologous with a nucleic acid sequence of the invention contained in the Sequence Listing.

In a preferred embodiment, the encoded *H. pylori* polypeptide differs (e.g., by amino acid substitution, addition or deletion of at least one amino acid residue) in amino acid sequence at 1, 2, 3, 5, 10 or more residues, from a sequence of the invention contained in the Sequence Listing. The differences, however, are such that: the *H*.

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pylori encoded polypeptide exhibits a H. pylori biological activity, e.g., the encoded H. pylori enzyme retains a biological activity of a naturally occurring H. pylori.

In preferred embodiments, the encoded polypeptide includes all or a fragment of an amino acid sequence of the invention contained in the Sequence Listing; fused, in reading frame, to additional amino acid residues, preferably to residues encoded by genomic DNA 5' or 3' to the genomic DNA which encodes a sequence of the invention contained in the Sequence Listing.

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In preferred embodiments, the subject *H. pylori* nucleic acid will include a transcriptional regulatory sequence, e.g. at least one of a transcriptional promoter or transcriptional enhancer sequence, operably linked to the *H. pylori* gene sequence, e.g., to render the *H. pylori* gene sequence suitable for expression in a recombinant host cell.

In yet a further preferred embodiment, the nucleic acid which encodes an *H. pylori* polypeptide of the invention, hybridizes under stringent conditions to a nucleic acid probe corresponding to at least 8 consecutive nucleotides of the invention contained in the Sequence Listing; more preferably to at least 12 consecutive nucleotides of the invention contained in the Sequence Listing; more preferably to at least 20 consecutive nucleotides of the invention contained in the Sequence Listing; more preferably to at least 40 consecutive nucleotides of the invention contained in the Sequence Listing.

In a preferred embodiment, the nucleic acid encodes a peptide which differs by at least one amino acid residue from the sequences of the invention contained in the Sequence Listing.

In a preferred embodiment, the nucleic acid differs by at least one nucleotide from a nucleotide sequence of the invention contained in the Sequence Listing which encodes amino acids of the invention contained in the Sequence Listing.

In another aspect, the invention encompasses: a vector including a nucleic acid which encodes an *H. pylori* polypeptide or an *H. pylori* polypeptide variant as described herein; a host cell transfected with the vector; and a method of producing a recombinant *H. pylori* polypeptide or *H. pylori* polypeptide variant; including culturing the cell, e.g., in a cell culture medium, and isolating the *H. pylori* or *H. pylori* polypeptide variant, e.g., from the cell or from the cell culture medium.

In another aspect, the invention features, a purified recombinant nucleic acid having at least 50%, 60%, 70%, 80%, 90%, 95%, 98%, or 99% homology with a sequence of the invention contained in the Sequence Listing.

The invention also provides a probe or primer which includes a substantially purified oligonucleotide. The oligonucleotide includes a region of nucleotide sequence which hybridizes under stringent conditions to at least 8 consecutive nucleotides of sense or antisense sequence of the invention contained in the Sequence Listing, or

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naturally occurring mutants thereof. In preferred embodiments, the probe or primer further includes a label group attached thereto. The label group can be, e.g., a radioisotope, a fluorescent compound, an enzyme, and/or an enzyme co-factor. Preferably the oligonucleotide is at least 8 and less than 10, 20, 30, 50, 100, or 150 nucleotides in length.

The invention also provides an isolated *H. pylori* polypeptide which is encoded by a nucleic acid which hybridizes under stringent hybridization conditions to a nucleic acid contained in the Sequence Listing.

The invention further provides nucleic acids, e.g., RNA or DNA, encoding a polypeptide of the invention. This includes double stranded nucleic acids as well as coding and antisense single strands.

The *H. pylori* strain, from which genomic sequences have been sequenced, has been deposited in the American Type Culture Collection (ATCC # 55679; deposited by Genome Therapeutics Corporation, 100 Beaver Street, Waltham, MA 02154) as strain HP-J99.

Included in the invention are: allelic variations; natural mutants; induced mutants; proteins encoded by DNA that hybridizes under high or low stringency conditions to a nucleic acid which encodes a polypeptide of the invention contained in the Sequence Listing (for definitions of high and low stringency see Current Protocols in Molecular Biology, John Wiley & Sons, New York, 1989, 6.3.1 - 6.3.6 and 6.4.1-6.4.10, hereby incorporated by reference); and, polypeptides specifically bound by antisera to *H. pylori* polypeptides, especially by antisera to an active site or binding domain of *H. pylori* polypeptide. The invention also includes fragments, preferably biologically active fragments. These and other polypeptides are also referred to herein as *H. pylori* polypeptide analogs or variants.

Putative functions have been determined for several of the *H. pylori* polypeptides of the invention, as shown in Table 1.

Accordingly, uses of the claimed *H. pylori* polypeptides based on these identified functions, as well as other functions as described herein, are also within the scope of the invention.

In addition, the present invention encompasses *H. pylori* polypeptides characterized as shown in Table 1 below, including: *H. pylori* cell envelope proteins, *H. pylori* secreted proteins, and *H. pylori* cellular proteins. Members of these groups were identified by BLAST homology searches and by searches for secretion signal or transmembrane protein motifs. Polypeptides related by significant homology to the polypeptides of Table 1 are also considered to be classified in the manner of the homologs shown in Table 1.

TABLE 1

ORF_Name and Group	nt SeqID	aa SeqID
A. CELL ENVELOPE	111 004.5	
A.1 Inner membrane proteins	 	
02ge11622_23494043_f1_6	3	- 76
hp5p15212_13095752_c3_36	25	
06ep30223_20173437_f1_37	48	
	40	121
A.2 Outer membrane proteins	40	83
05ee10816_14495437_f2_13	10	63
A.2.1 Terminal phe residue	10	
06ep11509_35954752_f2_1	16	
06ep10615_14495437_f3_47	45	
03ae10804_14495437_c2_38	35	I
05ae30220_917200_c3_172	37	
04cp11202_23646885_f2_26	7	
05ep10815_16131925_c2_97		
09cp61003_5860877_f2_23	55	
09ae10512_48768_c3_67	18	1
09cp11003_5860877_f3_7	19	92
hp6e12267_30478562_f3_33	28	101
06cp30603_34174212_c3_71	30	103
09cp10224_1962590_f3_31	52	125
09cp61003_30478562_c3_106	54	127
11ae80818_10553192_f2_16	56	129
11ee11408_10584582_c3_51	58	131
A.2.2 Terminal phe residue and C-		
terminal tyrosine cluster		
01ae12001_116018_c2_40	1	
06ap10609_116018_c3_50	42	115
06cp30603_4687507_f1_9	14	87
06cp30603_4687507_f1_7	43	116
05ee10816_36126938_f3_16	-11	84
01cp20708_4960952_c1_43	71	144
A.3 Via homolgy	Ti-	
07ap80601_5083193_f3_8	. 17	90
11ap20714_4797137_f3_45	57	130
A.4 Other cell envelope proteins	†	
04ap12016_25501501_f1_1	5	78
04cp11202_20415937_f2_25	6	
04ee11108_3906963_f1_7	8	
29ep10720_25501501_c2_33	21	1
B. SECRETED PROTEINS	+	+
hp3e10342 22448587_c2_15	72	145
	32	
hp5p15212_24276587_f1_2		
09ce10413_35336707_f2_9	51	124

01ae12001_32462543_c2_43	7 2	75
03ee11215_1416312_c3_35	4	
05ae30220_14570443_c2_94	9	
06cp30603_2772578_c1_46	13	
29ep10720_289077_f2_12	22	95
03ee11215_22542803 f1 7	29	102
09ae10512_3166040_c1_40	31	104
01ce11104_10742963_c2_12	33	104
02ge10116_36335436_f3_66	34	100
04ep41903_11876461_f1_4	36	107
05ce10208_23631292_f1_6	38	111
05ep10815_22447252_c3_110	40	113
05ep10815_30283516_c3_109	41	114
06ee30709_33851038_c3_30	44	117
06ep11202_21687842_c3_35	46	119
06ep30223_2774062_f1_33	49	122
09cp10713_23912707_c1_26	53	126
11ee11408_4882318_f3_24	59	132
hp4e13394 5908553 f1 1	61	134
hp4e53394_1416312_c3_119	62	135
hp5e15211_24328910_c3_38	63	136
hp6p10606_23493756_c1_21	65	138
hp6p22217_23564012_f1_5	66	139
hp6p22217_272058_f1_2	67	140
hp6p22217_2922143_f2_9	68	141
C. OTHER CELLULAR PROTEINS		
06ap11119_14726542_f3_21	12	85
06ee10709_6136430_c1_11	15	88
12ap10605_14094816_c1_5	20	93
hp2p10272_34042518_f1_2	23	96
hp5e15211_25411557_c1_22	24	97
hp5p15641_3907968_f1_3	26	99
hp6e10967_657638_f3_9	27	100
06ep11202_4569693_c2_28	47	120
06ep30223_3930468_c1_110	50	123
hp2e10911_960952_c2_86	60	133
hp6p10509_14642217_c2_17	64	137
hp6p80503_20964382_f2_11	69	142
hp7e10192_5917593_f1_2	70	143
hp6p10509_14642217_c3_25	73	146

[In Table 1, "nt" represents nucleotide Seq. ID number and "aa" represents amino acid Seq. ID number]

5 <u>Definitions</u>

The terms "purified polypeptide" and "isolated polypeptide" and "a substantially pure preparation of a polypeptide" are used interchangeably herein and, as used herein,

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from other proteins, lipids, and nucleic acids with which it naturally occurs. Preferably, the polypeptide is also separated from substances, e.g., antibodies or gel matrix, e.g., polyacrylamide, which are used to purify it. Preferably, the polypeptide constitutes at least 10, 20, 50 70, 80 or 95% dry weight of the purified preparation. Preferably, the preparation contains: sufficient polypeptide to allow protein sequencing; at least 1, 10, or 100 µg of the polypeptide; at least 1, 10, or 100 mg of the polypeptide. Furthermore, the terms "purified polypeptide" and "isolated polypeptide" and "a substantially pure preparation of a polypeptide," as used herein, refer to both a polypeptide obtained from nature or produced by recombinant DNA techniques as described herein.

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For example, an "isolated" or "purified" protein or biologically active portion thereof is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the H. pylori protein is derived, or substantially free from chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of H. pylori protein in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. In one embodiment, the language "substantially free of cellular material" includes preparations of H. pylori protein having less than about 30% (by dry weight) of non-H. pylori protein (also referred to herein as a "contaminating protein"), more preferably less than about 20% of non-H. pylori protein, still more preferably less than about 10% of non-H. pylori protein, and most preferably less than about 5% non-H. pylori protein. When the H. pylori protein or biologically active portion thereof is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture medium represents less than about 20%, more preferably less than about 10%, and most preferably less than about 5% of the volume of the protein preparation.

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The language "substantially free of chemical precursors or other chemicals" includes preparations of *H. pylori* protein in which the protein is separated from chemical precusors or other chemicals which are involved in the synthesis of the protein. In one embodiment, the language "substantially free of chemical precursors or other chemicals" includes preparations of *H. pylori* protein having less than about 30% (by dry weight) of chemical precursors or non-*H. pylori* chemicals, more preferably less than about 20% chemical precursors or non-*H. pylori* chemicals, still more preferably less than about 10% chemical precursors or non-*H. pylori* chemicals, and most preferably less than about 5% chemical precursors or non-*H. pylori* chemicals.

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A purified preparation of cells refers to, in the case of plant or animal cells, an *in* vitro preparation of cells and not an entire intact plant or animal. In the case of cultured

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cells or microbial cells, it consists of a preparation of at least 10% and more preferably 50% of the subject cells.

A purified or isolated or a substantially pure nucleic acid, e.g., a substantially pure DNA, (are terms used interchangeably herein) is a nucleic acid which is one or both of the following: not immediately contiguous with both of the coding sequences with which it is immediately contiguous (i.e., one at the 5' end and one at the 3' end) in the naturally-occurring genome of the organism from which the nucleic acid is derived; or which is substantially free of a nucleic acid with which it occurs in the organism from which the nucleic acid is derived. The term includes, for example, a recombinant DNA which is incorporated into a vector, e.g., into an autonomously replicating plasmid or virus, or into the genomic DNA of a prokaryote or eukaryote, or which exists as a separate molecule (e.g., a cDNA or a genomic DNA fragment produced by PCR or restriction endonuclease treatment) independent of other DNA sequences. Substantially pure DNA also includes a recombinant DNA which is part of a hybrid gene encoding additional *H. pylori* DNA sequence.

A "contig" as used herein is a nucleic acid representing a continuous stretch of genomic sequence of an organism.

An "open reading frame", also referred to herein as ORF, is a region of nucleic acid which encodes a polypeptide. This region may represent a portion of a coding sequence or a total sequence and can be determined from a stop to stop codon or from a start to stop codon.

As used herein, a "coding sequence" is a nucleic acid which is transcribed into messenger RNA and/or translated into a polypeptide when placed under the control of appropriate regulatory sequences. The boundaries of the coding sequence are determined by a translation start codon at the five prime terminus and a translation stop code at the three prime terminus. A coding sequence can include but is not limited to messenger RNA, synthetic DNA, and recombinant nucleic acid sequences.

A "complement" of a nucleic acid as used herein referes to an anti-parallel or antisense sequence that participates in Watson-Crick base-pairing with the original sequence.

A "gene product" is a protein or structural RNA which is specifically encoded by a gene.

As used herein, the term "probe" refers to a nucleic acid, peptide or other chemical entity which specifically binds to a molecule of interest. Probes are often associated with or capable of associating with a label. A label is a chemical moiety capable of detection. Typical labels comprise dyes, radioisotopes, luminescent and chemiluminescent moieties, fluorophores, enzymes, precipitating agents, amplification

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sequences, and the like. Similarly, a nucleic acid, peptide or other chemical entity which specifically binds to a molecule of interest and immobilizes such molecule is referred herein as a "capture ligand". Capture ligands are typically associated with or capable of associating with a support such as nitro-cellulose, glass, nylon membranes, beads, particles and the like. The specificity of hybridization is dependent on conditions such as the base pair composition of the nucleotides, and the temperature and salt concentration of the reaction. These conditions are readily discernable to one of ordinary skill in the art using routine experimentation.

Homologous refers to the sequence similarity or sequence identity between two polypeptides or between two nucleic acid molecules. When a position in both of the two compared sequences is occupied by the same base or amino acid monomer subunit, e.g., if a position in each of two DNA molecules is occupied by adenine, then the molecules are homologous at that position. The percent of homology between two sequences is a function of the number of matching or homologous positions shared by the two sequences divided by the number of positions compared x 100. For example, if 6 of 10 of the positions in two sequences are matched or homologous then the two sequences are 60% homologous. By way of example, the DNA sequences ATTGCC and TATGGC share 50% homology. Generally, a comparison is made when two sequences are aligned to give maximum homology.

Nucleic acids are hybridizable to each other when at least one strand of a nucleic acid can anneal to the other nucleic acid under defined stringency conditions. Stringency of hybridization is determined by: (a) the temperature at which hybridization and/or washing is performed; and (b) the ionic strength and polarity of the hybridization and washing solutions. Hybridization requires that the two nucleic acids contain complementary sequences; depending on the stringency of hybridization, however, mismatches may be tolerated. Typically, hybridization of two sequences at high stingency (such as, for example, in a solution of 0.5X SSC, at 65° C) requires that the sequences be essentially completely homologous. Conditions of intermediate stringency (such as, for example, 2X SSC at 65° C) and low stringency (such as, for example 2X SSC at 55° C), require correspondingly less overall complementarity between the hybridizing sequences. (1X SSC is 0.15 M NaCl, 0.015 M Na citrate). A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2 X SSC, 0.1% SDS at 50-65°C.

The terms peptides, proteins, and polypeptides are used interchangeably herein.

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As used herein, the term "surface protein" refers to all surface accessible proteins, e.g. inner and outer membrane proteins, proteins adhering to the cell wall, and secreted proteins.

A polypeptide has *H. pylori* biological activity if it has one, two and preferably more of the following properties: (1) if when expressed in the course of an *H. pylori* infection, it can promote, or mediate the attachment of *H. pylori* to a cell; (2) it has an enzymatic activity, structural or regulatory function characteristic of an *H. pylori* protein; (3) the gene which encodes it can rescue a lethal mutation in an *H. pylori* gene; (4) or it is immunogenic in a subject. A polypeptide has biological activity if it is an antagonist, agonist, or super-agonist of a polypeptide having one of the above-listed properties.

A biologically active fragment or analog is one having an *in vivo* or *in vitro* activity which is characteristic of the *H. pylori* polypeptides of the invention contained in the Sequence Listing, or of other naturally occurring *H. pylori* polypeptides, e.g., one or more of the biological activities described herein. Especially preferred are fragments which exist *in vivo*, e.g., fragments which arise from post transcriptional processing or which arise from translation of alternatively spliced RNA's. Fragments include those expressed in native or endogenous cells as well as those made in expression systems, e.g., in CHO cells. Because peptides such as *H. pylori* polypeptides often exhibit a range of physiological properties and because such properties may be attributable to different portions of the molecule, a useful *H. pylori* fragment or *H. pylori* analog is one which exhibits a biological activity in any biological assay for *H. pylori* activity. Most preferably the fragment or analog possesses 10%, preferably 40%, more preferably 60%, 70%, 80% or 90% or greater of the activity of *H. pylori*, in any *in vivo* or *in vitro* assay.

Analogs can differ from naturally occurring *H. pylori* polypeptides in amino acid sequence or in ways that do not involve sequence, or both. Non-sequence modifications include changes in acetylation, methylation, phosphorylation, carboxylation, or glycosylation. Preferred analogs include *H. pylori* polypeptides (or biologically active fragments thereof) whose sequences differ from the wild-type sequence by one or more conservative amino acid substitutions or by one or more non-conservative amino acid substitutions, deletions, or insertions which do not substantially diminish the biological activity of the *H. pylori* polypeptide. Conservative substitutions typically include the substitution of one amino acid for another with similar characteristics, e.g., substitutions within the following groups: valine, glycine; glycine, alanine; valine, isoleucine, leucine; aspartic acid, glutamic acid; asparagine, glutamine; serine, threonine; lysine, arginine; and phenylalanine, tyrosine. Other conservative substitutions can be made in view of the table below.

TABLE 2
CONSERVATIVE AMINO ACID REPLACEMENTS

For Amino Acid	Code	Replace with any of
Alanine	A	D-Ala, Gly, beta-Ala, L-Cys, D-Cys
Arginine	R	D-Arg, Lys, D-Lys, homo-Arg, D-homo-Arg, Met, Ile, D-Met, D-Ile, Orn, D-Orn
Asparagine	N	D-Asn, Asp, D-Asp, Glu, D-Glu, Gln, D-Gln
Aspartic Acid	D	D-Asp, D-Asn, Asn, Glu, D-Glu, Gln, D-Gln
Cysteine	C	D-Cys, S-Me-Cys, Met, D-Met, Thr, D-Thr
Glutamine	Q	D-Gln, Asn. D-Asn, Glu, D-Glu, Asp, D-Asp
Glutamic Acid	Е	D-Glu, D-Asp, Asp, Asn, D-Asn, Gln, D-Gln
Glycine	G	Ala, D-Ala, Pro, D-Pro, β-Ala, Acp
Isoleucine	I	D-Ile, Val, D-Val, Leu, D-Leu, Met, D-Met
Leucine	L	D-Leu, Val, D-Val, Leu, D-Leu, Met, D-Met
Lysine	K	D-Lys, Arg, D-Arg, homo-Arg, D-homo-Arg, Met, D-Met, Ile, D-Ile, Orn, D-Orn
Methionine	М	D-Met, S-Me-Cys, Ile, D-Ile, Leu, D-Leu, Val, D-Val
Phenylalanine	F	D-Phe, Tyr, D-Thr, L-Dopa, His, D-His, Trp, D-Trp, Trans-3,4, or 5-phenylproline, cis-3,4, or 5-phenylproline
Proline	P	D-Pro, L-I-thioazolidine-4-carboxylic acid, D-or L-1-oxazolidine-4-carboxylic acid
Serine	S	D-Ser, Thr, D-Thr, allo-Thr, Met, D-Met, Met(O), D-Met(O), L-Cys, D-Cys
Threonine	Т	D-Thr, Ser, D-Ser, allo-Thr, Met, D-Met, Met(O), D-Met(O), Val, D-Val
Tyrosine	Y	D-Tyr, Phe, D-Phe, L-Dopa, His, D-His
Valine	V	D-Val, Leu, D-Leu, Ile, D-Ile, Met, D-Met

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Other analogs within the invention are those with modifications which increase peptide stability; such analogs may contain, for example, one or more non-peptide bonds (which replace the peptide bonds) in the peptide sequence. Also included are: analogs that include residues other than naturally occurring L-amino acids, e.g., D-amino acids or non-naturally occurring or synthetic amino acids, e.g., β or γ amino acids; and cyclic analogs.

As used herein, the term "fragment", as applied to an *H. pylori* analog, will ordinarily be at least about 20 residues, more typically at least about 40 residues, preferably at least about 60 residues in length. Fragments of *H. pylori* polypeptides can be generated by methods known to those skilled in the art. The ability of a candidate fragment to exhibit a biological activity of *H. pylori* polypeptide can be assessed by methods known to those skilled in the art as described herein. Also included are *H. pylori* polypeptides containing residues that are not required for biological activity of the peptide or that result from alternative mRNA splicing or alternative protein processing events.

An "immunogenic component" as used herein is a moiety, such as an *H. pylori* polypeptide, analog or fragment thereof, that is capable of eliciting a humoral and/or cellular immune response in a host animal alone or in combination with an adjuvant.

An "antigenic component" as used herein is a moiety, such as an *H. pylori* polypeptide, analog or fragment thereof, that is capable of binding to a specific antibody with sufficiently high affinity to form a detectable antigen-antibody complex.

As used herein, the term "transgene" means a nucleic acid (encoding, e.g., one or more polypeptides), which is partly or entirely heterologous, i.e., foreign, to the transgenic animal or cell into which it is introduced, or, is homologous to an endogenous gene of the transgenic animal or cell into which it is introduced, but which is designed to be inserted, or is inserted, into the cell's genome in such a way as to alter the genome of the cell into which it is inserted (e.g., it is inserted at a location which differs from that of the natural gene or its insertion results in a knockout). A transgene can include one or more transcriptional regulatory sequences and any other nucleic acid, such as introns, that may be necessary for optimal expression of the selected nucleic acid, all operably linked to the selected nucleic acid, and may include an enhancer sequence.

As used herein, the term "transgenic cell" refers to a cell containing a transgene. As used herein, a "transgenic animal" is any animal in which one or more, and preferably essentially all, of the cells of the animal includes a transgene. The transgene can be introduced into the cell, directly or indirectly by introduction into a precursor of the cell, by way of deliberate genetic manipulation, such as by a process of transformation of competent cells or by microinjection or by infection with a

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recombinant virus. This molecule may be integrated within a chromosome, or it may be extrachromosomally replicating DNA.

The term "antibody" as used herein is intended to include fragments thereof which are specifically reactive with *H. pylori* polypeptides.

As used herein, the term "cell-specific promoter" means a DNA sequence that serves as a promoter, i.e., regulates expression of a selected DNA sequence operably linked to the promoter, and which effects expression of the selected DNA sequence in specific cells of a tissue. The term also covers so-called "leaky" promoters, which regulate expression of a selected DNA primarily in one tissue, but cause expression in other tissues as well.

Misexpression, as used herein, refers to a non-wild type pattern of gene expression. It includes: expression at non-wild type levels, i.e., over or under expression; a pattern of expression that differs from wild type in terms of the time or stage at which the gene is expressed, e.g., increased or decreased expression (as compared with wild type) at a predetermined developmental period or stage; a pattern of expression that differs from wild type in terms of decreased expression (as compared with wild type) in a predetermined cell type or tissue type; a pattern of expression that differs from wild type in terms of the splicing size, amino acid sequence, post-transitional modification, or biological activity of the expressed polypeptide; a pattern of expression that differs from wild type in terms of the effect of an environmental stimulus or extracellular stimulus on expression of the gene, e.g., a pattern of increased or decreased expression (as compared with wild type) in the presence of an increase or decrease in the strength of the stimulus.

As used herein, "host cells" and other such terms denoting microorganisms or higher eukaryotic cell lines cultured as unicellular entities refers to cells which can become or have been used as recipients for a recombinant vector or other transfer DNA, and include the progeny of the original cell which has been transfected. It is understood by individuals skilled in the art that the progeny of a single parental cell may not necessarily be completely identical in genomic or total DNA compliment to the original parent, due to accident or deliberate mutation.

As used herein, the term "control sequence" refers to a nucleic acid having a base sequence which is recognized by the host organism to effect the expression of encoded sequences to which they are ligated. The nature of such control sequences differs depending upon the host organism; in prokaryotes, such control sequences generally include a promoter, ribosomal binding site, terminators, and in some cases operators; in eukaryotes, generally such control sequences include promoters, terminators and in some instances, enhancers. The term control sequence is intended to include at a

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minimum, all components whose presence is necessary for expression, and may also include additional components whose presence is advantageous, for example, leader sequences.

As used herein, the term "operably linked" refers to sequences joined or ligated to function in their intended manner. For example, a control sequence is operably linked to coding sequence by ligation in such a way that expression of the coding sequence is achieved under conditions compatible with the control sequence and host cell.

The metabolism of a substance, as used herein, means any aspect of the, expression, function, action, or regulation of the substance. The metabolism of a substance includes modifications, e.g., covalent or non-covalent modifications of the substance. The metabolism of a substance includes modifications, e.g., covalent or non-covalent modification, the substance induces in other substances. The metabolism of a substance also includes changes in the distribution of the substance. The metabolism of a substance includes changes the substance induces in the distribution of other substances.

A "sample" as used herein refers to a biological sample, such as, for example, tissue or fluid isloated from an individual (including without limitation plasma, serum, cerebrospinal fluid, lymph, tears, saliva and tissue sections) or from *in vitro* cell culture constituents, as well as samples from the environment.

The practice of the invention will employ, unless otherwise indicated, conventional techniques of chemistry, molecular biology, microbiology, recombinant DNA, and immunology, which are within the skill of the art. Such techniques are explained fully in the literature. See e.g., Sambrook, Fritsch, and Maniatis, Molecular Cloning; Laboratory Manual 2nd ed. (1989); DNA Cloning, Volumes I and II (D.N Glover ed. 1985); Oligonucleotide Synthesis (M.J. Gait ed, 1984); Nucleic Acid Hybridization (B.D. Hames & S.J. Higgins eds. 1984); the series, Methods in Enzymology (Academic Press, Inc.), particularly Vol. 154 and Vol. 155 (Wu and Grossman, eds.) and PCR-A Practical Approach (McPherson, Quirke, and Taylor, eds., 1991).

I. Isolation of Nucleic Acids of H. pylori and Uses Therefor

H. pylori Genomic Sequence

This invention provides nucleotide sequences of the genome of *H. pylori* which thus comprises a DNA sequence library of *H. pylori* genomic DNA. The detailed description that follows provides nucleotide sequences of *H. pylori*, and also describes how the sequences were obtained and how ORFs and protein-coding sequences were

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identified. Also described are methods of using the disclosed *H. pylori* sequences in methods including diagnostic and therapeutic applications. Furthermore, the library can be used as a database for identification and comparison of medically important sequences in this and other strains of *H. pylori*.

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To determine the genomic sequence of *H. pylori*, DNA was isolated from a strain of *H. pylori* (ATCC # 55679; deposited by Genome Therapeutics Corporation, 100 Beaver Street, Waltham, MA 02154) and mechanically sheared by nebulization to a median size of 2 kb. Following size fractionation by gel electrophoresis, the fragments were blunt-ended, ligated to adapter oligonucleotides, and cloned into each of 20 different pMPX vectors (Rice et al., abstracts of Meeting of Genome Mapping and Sequencing, Cold Spring Harbor, NY, 5/11-5/15, 1994, p. 225) to construct a series of "shotgun" subclone libraries.

DNA sequencing was achieved using multiplex sequencing procedures essentially as disclosed in Church et al., 1988, *Science* 240:185; U.S. Patents No. 4,942,124 and 5,149,625). DNA was extracted from pooled cultures and subjected to chemical or enzymatic sequencing. Sequencing reactions were resolved by electrophoresis, and the products were transferred and covalently bound to nylon membranes. Finally, the membranes were sequentially hybridized with a series of labelled oligonucleotides complimentary to "tag" sequences present in the different shotgun cloning vectors. In this manner, a large number of sequences could be obtained from a single set of sequencing reactions. The cloning and sequencing procedures are described in more detail in the Exemplification.

Individual sequence reads obtained in this manner were assembled using the FALCONTM program (Church *et al.*, 1994, *Automated DNA Sequencing and Analysis*, J.C. Venter, ed., Academic Press) and PHRAP (P. Green, Abstracts of DOE Human Genome Program Contractor-Grantee Workshop V, Jan. 1996, p.157). The average contig length was about 3-4 kb.

A variety of approaches are used to order the contigs so as to obtain a continuous sequence representing the entire *H. pylori* genome. Synthetic oligonucleotides are designed that are complementary to sequences at the end of each contig. These oligonucleotides may be hybridized to libaries of *H. pylori* genomic DNA in, for example, lambda phage vectors or plasmid vectors to identify clones that contain sequences corresponding to the junctional regions between individual contigs. Such clones are then used to isolate template DNA and the same oligonucleotides are used as primers in polymerase chain reaction (PCR) to amplify junctional fragments, the nucleotide sequence of which is then determined.

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The *H. pylori* sequences were analyzed for the presence of open reading frames (ORFs) comprising at least 180 nucleotides. As a result of the analysis of ORFs based on stop-to-stop codon reads, it should be understood that these ORFs may not correspond to the ORF of a naturally-occurring *H. pylori* polypeptide. These ORFs may contain start codons which indicate the initiation of protein synthesis of a naturally-occurring *H. pylori* polypeptide. Such start codons within the ORFs provided herein can be identified by those of ordinary skill in the relevant art, and the resulting ORF and the encoded *H. pylori* polypeptide is within the scope of this invention. For example, within the ORFs a codon such as AUG or GUG (encoding methionine or valine) which is part of the initiation signal for protein synthesis can be identified and the ORF modified to correspond to a naturally-occurring *H. pylori* polypeptide. The predicted coding regions were defined by evaluating the coding potential of such sequences with the program GENEMARKTM (Borodovsky and McIninch, 1993, *Comp. Chem.* 17:123).

15 Other H. pylori Nucleic Acids

The nucleic acids of this invention may be obtained directly from the DNA of the above referenced *H. pylori* strain by using the polymerase chain reaction (PCR). See "PCR, A Practical Approach" (McPherson, Quirke, and Taylor, eds., IRL Press, Oxford, UK, 1991) for details about the PCR. High fidelity PCR can be used to ensure a faithful DNA copy prior to expression. In addition, the authenticity of amplified products can be checked by conventional sequencing methods. Clones carrying the desired sequences described in this invention may also be obtained by screening the libraries by means of the PCR or by hybridization of synthetic oligonucleotide probes to filter lifts of the library colonies or plaques as known in the art (see, e.g., Sambrook et al., *Molecular Cloning, A Laboratory Manual* 2nd edition, 1989, Cold Spring Harbor Press, NY).

It is also possible to obtain nucleic acids encoding *H. pylori* polypeptides from a cDNA library in accordance with protocols herein described. A cDNA encoding an *H. pylori* polypeptide can be obtained by isolating total mRNA from an appropriate strain. Double stranded cDNAs can then be prepared from the total mRNA. Subsequently, the cDNAs can be inserted into a suitable plasmid or viral (e.g., bacteriophage) vector using any one of a number of known techniques. Genes encoding *H. pylori* polypeptides can also be cloned using established polymerase chain reaction techniques in accordance with the nucleotide sequence information provided by the invention. The nucleic acids of the invention can be DNA or RNA. Preferred nucleic acids of the invention are contained in the Sequence Listing.

The nucleic acids of the invention can also be chemically synthesized using standard techniques. Various methods of chemically synthesizing polydeoxynucleotides

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are known, including solid-phase synthesis which, like peptide synthesis, has been fully automated in commercially available DNA synthesizers (See e.g., Itakura et al. U.S. Patent No. 4,598,049; Caruthers et al. U.S. Patent No. 4,458,066; and Itakura U.S. Patent Nos. 4,401,796 and 4,373,071, incorporated by reference herein).

Nucleic acids isolated or synthesized in accordance with features of the present invention are useful, by way of example, without limitation, as probes, primers, capture ligands, antisense genes and for developing expression systems for the synthesis of proteins and peptides corresponding to such sequences. As probes, primers, capture ligands and antisense agents, the nucleic acid normally consists of all or part (approximately twenty or more nucleotides for specificity as well as the ability to form stable hybridization products) of the nucleic acids of the invention contained in the Sequence Listing. These uses are described in further detail below.

Probes

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A nucleic acid isolated or synthesized in accordance with the sequence of the invention contained in the Sequence Listing can be used as a probe to specifically detect *H. pylori*. With the sequence information set forth in the present application, sequences of twenty or more nucleotides are identified which provide the desired inclusivity and exclusivity with respect to *H. pylori*, and extraneous nucleic acids likely to be encountered during hybridization conditions. More preferably, the sequence will comprise at least twenty to thirty nucleotides to convey stability to the hybridization product formed between the probe and the intended target molecules.

Sequences larger than 1000 nucleotides in length are difficult to synthesize but can be generated by recombinant DNA techniques. Individuals skilled in the art will readily recognize that the nucleic acids, for use as probes, can be provided with a label to facilitate detection of a hybridization product.

Nucleic acid isolated and synthesized in accordance with the sequence of the invention contained in the Sequence Listing can also be useful as probes to detect homologous regions (especially homologous genes) of other *Helicobacter* species using appropriate stringency hybridization conditions as described herein.

Capture Ligand

For use as a capture ligand, the nucleic acid selected in the manner described above with respect to probes, can be readily associated with a support. The manner in which nucleic acid is associated with supports is well known. Nucleic acid having twenty or more nucleotides in a sequence of the invention contained in the Sequence Listing have utility to separate *H. pylori* nucleic acid from the nucleic acid of each other and other organisms. Nucleic acid having twenty or more nucleotides in a sequence of the invention contained in the Sequence Listing can also have utility to separate other

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Helicobacter species from each other and from other organisms. Preferably, the sequence will comprise at least twenty nucleotides to convey stability to the hybridization product formed between the probe and the intended target molecules. Sequences larger than 1000 nucleotides in length are difficult to synthesize but can be generated by recombinant DNA techniques.

Primers

Nucleic acid isolated or synthesized in accordance with the sequences described herein have utility as primers for the amplification of H. pylori nucleic acid. These nucleic acids may also have utility as primers for the amplification of nucleic acids in other Helicobacter species. With respect to polymerase chain reaction (PCR) techniques, nucleic acid sequences of ≥ 10 -15 nucleotides of the invention contained in the Sequence Listing have utility in conjunction with suitable enzymes and reagents to create copies of H. pylori nucleic acid. More preferably, the sequence will comprise twenty or more nucleotides to convey stability to the hybridization product formed between the primer and the intended target molecules. Binding conditions of primers greater than 100 nucleotides are more difficult to control to obtain specificity. High fidelity PCR can be used to ensure a faithful DNA copy prior to expression. In addition, amplified products can be checked by conventional sequencing methods.

The copies can be used in diagnostic assays to detect specific sequences, including genes from *H. pylori* and/or other *Helicobacter* species. The copies can also be incorporated into cloning and expression vectors to generate polypeptides corresponding to the nucleic acid synthesized by PCR, as is described in greater detail herein.

<u>Antisense</u>

Nucleic acid or nucleic acid-hybridizing derivatives isolated or synthesized in accordance with the sequences described herein have utility as antisense agents to prevent the expression of *H. pylori* genes. These sequences also have utility as antisense agents to prevent expression of genes of other *Helicobacter* species.

In one embodiment, nucleic acid or derivatives corresponding to *H. pylori* nucleic acids is loaded into a suitable carrier such as a liposome or bacteriophage for introduction into bacterial cells. For example, a nucleic acid having twenty or more nucleotides is capable of binding to bacteria nucleic acid or bacteria messenger RNA. Preferably, the antisense nucleic acid is comprised of 20 or more nucleotides to provide necessary stability of a hybridization product of non-naturally occurring nucleic acid and bacterial nucleic acid and/or bacterial messenger RNA. Nucleic acid having a sequence greater than 1000 nucleotides in length is difficult to synthesize but can be generated by recombinant DNA techniques. Methods for loading antisense nucleic acid in liposomes

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is known in the art as exemplified by U.S. Patent 4,241,046 issued December 23, 1980 to Papahadjopoulos et al.

II. Expression of H. pylori Nucleic Acids

Nucleic acid isolated or synthesized in accordance with the sequences described herein have utility to generate polypeptides. The nucleic acid of the invention exemplified in the Sequence Listing or fragments of said nucleic acid encoding active portions of *H. pylori* polypeptides can be cloned into suitable vectors or used to isolate nucleic acid. The isolated nucleic acid is combined with suitable DNA linkers and cloned into a suitable vector.

The function of a specific gene or operon can be ascertained by expression in a bacterial strain under conditions where the activity of the gene product(s) specified by the gene or operon in question can be specifically measured. Alternatively, a gene product may be produced in large quantities in an expressing strain for use as an antigen, an industrial reagent, for structural studies, etc. This expression can be accomplished in a mutant strain which lacks the activity of the gene to be tested, or in a strain that does not produce the same gene product(s). This includes, but is not limited to other Helicobacter strains, or other bacterial strains such as E. coli, Norcardia, Corynebacterium, Campylobacter, and Streptomyces species. In some cases the expression host will utilize the natural Helicobacter promoter whereas in others, it will be necessary to drive the gene with a promoter sequence derived from the expressing organism (e.g., an E. coli beta-galactosidase promoter for expression in E. coli).

To express a gene product using the natural *H. pylori* promoter, a procedure such as the following can be used. A restriction fragment containing the gene of interest, together with its associated natural promoter element and regulatory sequences (identified using the DNA sequence data) is cloned into an appropriate recombinant plasmid containing an origin of replication that functions in the host organism and an appropriate selectable marker. This can be accomplished by a number of procedures known to those skilled in the art. It is most preferably done by cutting the plasmid and the fragment to be cloned with the same restriction enzyme to produce compatible ends that can be ligated to join the two pieces together. The recombinant plasmid is introduced into the host organism by, for example, electroporation and cells containing the recombinant plasmid are identified by selection for the marker on the plasmid. Expression of the desired gene product is detected using an assay specific for that gene product.

In the case of a gene that requires a different promoter, the body of the gene (coding sequence) is specifically excised and cloned into an appropriate expression

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plasmid. This subcloning can be done by several methods, but is most easily accomplished by PCR amplification of a specific fragment and ligation into an expression plasmid after treating the PCR product with a restriction enzyme or exonuclease to create suitable ends for cloning.

A suitable host cell for expression of a gene can be any procaryotic or eucaryotic cell. For example, an *H. pylori* polypeptide can be expressed in bacterial cells such as *E. coli*, insect cells (baculovirus), yeast, or mammalian cells such as Chinese hamster ovary cell (CHO). Other suitable host cells are known to those skilled in the art.

Expression in eucaryotic cells such as mammalian, yeast, or insect cells can lead to partial or complete glycosylation and/or formation of relevant inter- or intra-chain 10 disulfide bonds of a recombinant peptide product. Examples of vectors for expression in yeast S. cerivisae include pYepSec1 (Baldari. et al., (1987) Embo J. 6:229-234), pMFa (Kurjan and Herskowitz, (1982) Cell 30:933-943), pJRY88 (Schultz et al., (1987) Gene 54:113-123), and pYES2 (Invitrogen Corporation, San Diego, CA). Baculovirus vectors available for expression of proteins in cultured insect cells (SF 9 cells) include the pAc 15 series (Smith et al., (1983) Mol. Cell Biol. 3:2156-2165) and the pVL series (Lucklow, V.A., and Summers, M.D., (1989) Virology 170:31-39). Generally, COS cells (Gluzman, Y., (1981) Cell 23:175-182) are used in conjunction with such vectors as pCDM 8 (Aruffo, A. and Seed, B., (1987) Proc. Natl. Acad. Sci. USA 84:8573-8577) for transient amplification/expression in mammalian cells, while CHO (dhfr-Chinese 20 Hamster Ovary) cells are used with vectors such as pMT2PC (Kaufman et al. (1987), EMBO J. 6:187-195) for stable amplification/expression in mammalian cells. Vector DNA can be introduced into mammalian cells via conventional techniques such as calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection, or electroporation. Suitable methods for transforming host cells can be 25 found in Sambrook et al. (Molecular Cloning: A Laboratory Manual, 2nd Edition, Cold Spring Harbor Laboratory press (1989)), and other laboratory textbooks.

Expression in procaryotes is most often carried out in *E. coli* with either fusion or non-fusion inducible expression vectors. Fusion vectors usually add a number of NH₂ terminal amino acids to the expressed target gene. These NH₂ terminal amino acids often are referred to as a reporter group. Such reporter groups usually serve two purposes: 1) to increase the solubility of the target recombinant protein; and 2) to aid in the purification of the target recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the reporter group and the target recombinant protein to enable separation of the target recombinant protein from the reporter group subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition

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sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors include pGEX (Amrad Corp., Melbourne, Australia), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase, maltose E binding protein, or protein A, respectively, to the target recombinant protein. A preferred reporter group is poly(His), which may be fused to the amino or carboxy terminus of the protein and which renders the recombinant fusion protein easily purifiable by metal chelate chromatography.

Inducible non-fusion expression vectors include pTrc (Amann et al., (1988) Gene 69:301-315) and pET11d (Studier et al., Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, California (1990) 60-89). While target gene expression relies on host RNA polymerase transcription from the hybrid trp-lac fusion promoter in pTrc, expression of target genes inserted into pET11d relies on transcription from the T7 gn10-lac 0 fusion promoter mediated by coexpressed viral RNA polymerase (T7 gn1). This viral polymerase is supplied by host strains BL21(DE3) or HMS174(DE3) from a resident λ prophage harboring a T7 gn1 under the transcriptional control of the lacUV 5 promoter.

For example, a host cell transfected with a nucleic acid vector directing expression of a nucleotide sequence encoding an *H. pylori* polypeptide can be cultured under appropriate conditions to allow expression of the polypeptide to occur. The polypeptide may be secreted and isolated from a mixture of cells and medium containing the peptide. Alternatively, the polypeptide may be retained cytoplasmically and the cells harvested, lysed and the protein isolated. A cell culture includes host cells, media and other byproducts. Suitable media for cell culture are well known in the art. Polypeptides of the invention can be isolated from cell culture medium, host cells, or both using techniques known in the art for purifying proteins including ion-exchange chromatography, gel filtration chromatography, ultrafiltration, electrophoresis, and immunoaffinity purification with antibodies specific for such polypeptides. Additionally, in many situations, polypeptides can be produced by chemical cleavage of a native protein (e.g., tryptic digestion) and the cleavage products can then be purified by standard techniques.

In the case of membrane bound proteins, these can be isolated from a host cell by contacting a membrane-associated protein fraction with a detergent forming a solubilized complex, where the membrane-associated protein is no longer entirely embedded in the membrane fraction and is solubilized at least to an extent which allows it to be chromatographically isolated from the membrane fraction. Several different criteria are used for choosing a detergent suitable for solubilizing these complexes. For example, one property considered is the ability of the detergent to solubilize the *H*.

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pylori protein within the membrane fraction at minimal denaturation of the membraneassociated protein allowing for the activity or functionality of the membrane-associated protein to return upon reconstitution of the protein. Another property considered when selecting the detergent is the critical micelle concentration (CMC) of the detergent in that the detergent of choice preferably has a high CMC value allowing for ease of removal after reconstitution. A third property considered when selecting a detergent is the hydrophobicity of the detergent. Typically, membrane-associated proteins are very hydrophobic and therefore detergents which are also hydrophobic, e.g., the triton series, would be useful for solubilizing the hydrophobic proteins. Another property important to a detergent can be the capability of the detergent to remove the H. pylori protein with minimal protein-protein interaction facilitating further purification. A fifth property of the detergent which should be considered is the charge of the detergent. For example, if it is desired to use ion exchange resins in the purification process then preferably detergent should be an uncharged detergent. Chromatographic techniques which can be used in the final purification step are known in the art and include hydrophobic interaction, lectin affinity, ion exchange, dye affinity and immunoaffinity.

One strategy to maximize recombinant *H. pylori* peptide expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the recombinant protein (Gottesman, S., Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, California (1990) 119-128). Another strategy would be to alter the nucleic acid encoding an *H. pylori* peptide to be inserted into an expression vector so that the individual codons for each amino acid would be those preferentially utilized in highly expressed *E. coli* proteins (Wada et al., (1992) *Nuc. Acids Res.* 20:2111-2118). Such alteration of nucleic acids of the invention can be carried out by standard DNA synthesis techniques.

The nucleic acids of the invention can also be chemically synthesized using standard techniques. Various methods of chemically synthesizing polydeoxynucleotides are known, including solid-phase synthesis which, like peptide synthesis, has been fully automated in commercially available DNA synthesizers (See, e.g., Itakura et al. U.S. Patent No. 4,598,049; Caruthers et al. U.S. Patent No. 4,458,066; and Itakura U.S. Patent Nos. 4,401,796 and 4,373,071, incorporated by reference herein).

III. H. pylori Polypeptides

This invention encompasses isolated *H. pylori* polypeptides encoded by the disclosed *H. pylori* genomic sequences, including the polypeptides of the invention contained in the Sequence Listing. Polypeptides of the invention are preferably at least 5 amino acid residues in length. Using the DNA sequence information provided herein,

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the amino acid sequences of the polypeptides encompassed by the invention can be deduced using methods well-known in the art. It will be understood that the sequence of an entire nucleic acid encoding an *H. pylori* polypeptide can be isolated and identified based on an ORF that encodes only a fragment of the cognate protein-coding region. This can be acheived, for example, by using the isolated nucleic acid encoding the ORF, or fragments thereof, to prime a polymerase chain reaction with genomic *H. pylori* DNA as template; this is followed by sequencing the amplified product.

The polypeptides of the invention can be isolated from wild-type or mutant *H. pylori* cells or from heterologous organisms or cells (including, but not limited to, bacteria, yeast, insect, plant and mammalian cells) into which an *H. pylori* nucleic acid has been introduced and expressed. In addition, the polypeptides can be part of recombinant fusion proteins.

H. pylori polypeptides of the invention can be chemically synthesized using commercially automated procedures such as those referenced herein.

IV. Identification of Nucleic Acids Encoding Vaccine Components and Targets for Agents Effective Against H. pylori

The disclosed *H. pylori* genome sequence includes segments that direct the synthesis of ribonucleic acids and polypeptides, as well as origins of replication, promoters, other types of regulatory sequences, and intergenic nucleic acids. The invention encompasses nucleic acids encoding immunogenic components of vaccines and targets for agents effective against *H. pylori*. Identification of said immunogenic components involved in the determination of the function of the disclosed sequences can be achieved using a variety of approaches. Non-limiting examples of these approaches are described briefly below.

Homology to known sequences: Computer-assisted comparison of the disclosed *H. pylori* sequences with previously reported sequences present in publicly available databases is useful for identifying functional *H. pylori* nucleic acid and polypeptide sequences. It will be understood that protein-coding sequences, for example, may be compared as a whole, and that a high degree of sequence homology between two proteins (such as, for example, >80-90%) at the amino acid level indicates that the two proteins also possess some degree of functional homology, such as, for example, among enzymes involved in metabolism, DNA synthesis, or cell wall synthesis, and proteins involved in transport, cell division, etc. In addition, many structural features of particular protein classes have been identified and correlate with specific consensus sequences, such as, for example, binding domains for nucleotides, DNA, metal ions, and other small molecules; sites for covalent modifications such as phosphorylation,

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acylation, and the like; sites of protein:protein interactions, etc. These consensus sequences may be quite short and thus may represent only a fraction of the entire protein-coding sequence. Identification of such a feature in an *H. pylori* sequence is therefore useful in determining the function of the encoded protein and identifying useful targets of antibacterial drugs.

Of particular relevance to the present invention are structural features that are common to secretory, transmembrane, and surface proteins, including secretion signal peptides and hydrophobic transmembrane domains. *H. pylori* proteins identified as containing putative signal sequences and/or transmembrane domains are useful as immunogenic components of vaccines.

Identification of essential genes: Nucleic acids that encode proteins essential for growth or viability of *H. pylori* are preferred drug targets. *H. pylori* genes can be tested for their biological relevance to the organism by examining the effect of deleting and/or disrupting the genes, i.e., by so-called gene "knockout", using techniques known to those skilled in the relevant art. In this manner, essential genes may be identified.

Strain-specific sequences: Because of the evolutionary relationship between different *H. pylori* strains, it is believed that the presently disclosed *H. pylori* sequences are useful for identifying, and/or discriminating between, previously known and new *H. pylori* strains. It is believed that other *H. pylori* strains will exhibit at least 70% sequence homology with the presently disclosed sequence. Systematic and routine analyses of DNA sequences derived from samples containing *H. pylori* strains, and comparison with the present sequence allows for the identification of sequences that can be used to discriminate between strains, as well as those that are common to all *H. pylori* strains. In one embodiment, the invention provides nucleic acids, including probes, and peptide and polypeptide sequences that discriminate between different strains of *H. pylori*. Strain-specific components can also be identified functionally by their ability to elicit or react with antibodies that selectively recognize one or more *H. pylori* strains.

In another embodiment, the invention provides nucleic acids, including probes, and peptide and polypeptide sequences that are common to all *H. pylori* strains but are *not* found in other bacterial species.

Specific Example: Determination Of Candidate Protein Antigens For Antibody And Vaccine Development

The selection of candidate protein antigens for vaccine development can be derived from the nucleic acids encoding *H. pylori* polypeptides. First, the ORF's can be analyzed for homology to other known exported or membrane proteins and analyzed using the discriminant analysis described by Klein, et al. (Klein, P., Kanehsia, M., and

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DeLisi, C. (1985) *Biochimica et Biophysica Acta* 815, 468-476) for predicting exported and membrane proteins.

Homology searches can be performed using the BLAST algorithm contained in the Wisconsin Sequence Analysis Package (Genetics Computer Group, University Research Park, 575 Science Drive, Madison, WI 53711) to compare each predicted ORF amino acid sequence with all sequences found in the current GenBank, SWISS-PROT and PIR databases. BLAST searches for local alignments between the ORF and the databank sequences and reports a probability score which indicates the probability of finding this sequence by chance in the database. ORF's with significant homology (e.g. probabilities lower than 1x10-6 that the homology is only due to random chance) to membrane or exported proteins represent protein antigens for vaccine development. Possible functions can be provided to *H. pylori* genes based on sequence homology to genes cloned in other organisms.

Discriminant analysis (Klein, et al. supra) can be used to examine the ORF amino acid sequences. This algorithm uses the intrinsic information contained in the ORF amino acid sequence and compares it to information derived from the properties of known membrane and exported proteins. This comparison predicts which proteins will be exported, membrane associated or cytoplasmic. ORF amino acid sequences identified as exported or membrane associated by this algorithm are likely protein antigens for vaccine development.

Surface exposed outer membrane proteins are likely to represent the best antigens to provide a protective immune response against *H. pylori*. Among the algorithms that can be used to aid in prediction of these outer membrane proteins include the presence of an amphipathic beta-sheet region at their C-terminus. This region which has been detected in a large number of outer membrane proteins in Gram negative bacteria is often characterized by hydrophobic residues (Phe or Tyr) clustered at alternating positions from the C-terminus (e.g., see Figure 5, block F; Figure 7, block E). Importantly, these sequences have not been detected at the C-termini of periplasmic proteins, thus allowing preliminary distinction between these classes of proteins based on primary sequence data. This phenomenon has been reported previously by Struyve et al. (*J. Mol. Biol.* 218:141-148, 1991).

Also illustrated in Figure 5 are additional amino acid sequence motifs found in many outer membrane proteins of *H. pylori*. The amino acid sequence alignment in Figure 5 depicts portions of the sequence of five *H. pylori* proteins (depicted in the single letter amino acid code) labeled with their amino acid Sequence ID Numbers and shown N-terminal to C-terminal, left to right. Five or six distinct blocks (labeled A through E or F) of similar amino acid residues are found including the distinctive

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hydrophobic residues (Phe or Tyr; F or Y according to the single letter code for amino acid residues) frequently found at positions near the C-terminus of outer membrane proteins. The presence of several shared motifs clearly establishes the similarity between members of this group of proteins.

Additional amino acid alignments for four outer membrane proteins isolated from *H. pylori* are depicted in Figure 6.

Outer membrane proteins isolated from *H. pylori* frequently share additional motifs as depicted for two proteins in Figure 7 which also share the C-terminal hydrophobic residues, and as depicted for two proteins in Figure 8 which do not share the C-terminal hydrophobic residue motif but share a different C-terminal motif.

One skilled in the art would know that these shared sequence motifs are highly significant and establish a similarity among this group of proteins.

Infrequently it is not possible to distinguish between multiple possible nucleotides at a given position in the nucleic acid sequence. In those cases the ambiguities are denoted by an extended alphabet as follows:

These are the official IUPAC-IUB single-letter base codes

Code	Base Description	·
G	Guanine	
A	Adenine	
T	Thymine	
C	Cytosine	·
R	Purine	(A or G)
Y	Pyrimidine	(C or T or U)
M	Amino	(A or C)
K	Ketone	(G or T)
S	Strong interaction	(C or G)
W	Weak interaction	(A or T)
Н	Not-G	(A or C or T)
В	Not-A	(C or G or T)
· V ,	Not-T (not-U)	(A or C or G)
D .	Not-C	(A or G or T)
N	Any	(A or C or G or T)

The amino acid translations of this invention account for the ambiguity in the nucleic acid sequence by translating the ambiguous codon as the letter "X". In all cases,

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the permissible amino acid residues at a position are clear from an examination of the nucleic acid sequence based on the standard genetic code.

V. Production of Fragments and Analogs of H. pylori Nucleic Acids and Polypeptides

Based on the discovery of the *H. pylori* gene products of the invention provided in the Sequence Lsiting, one skilled in the art can alter the disclosed structure (of *H. pylori* genes), e.g., by producing fragments or analogs, and test the newly produced structures for activity. Examples of techniques known to those skilled in the relevant art which allow the production and testing of fragments and analogs are discussed below. These, or analogous methods can be used to make and screen libraries of polypeptides, e.g., libraries of random peptides or libraries of fragments or analogs of cellular proteins for the ability to bind *H. pylori* polypeptides. Such screens are useful for the identification of inhibitors of *H. pylori*.

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Fragments of a protein can be produced in several ways, e.g., recombinantly, by proteolytic digestion, or by chemical synthesis. Internal or terminal fragments of a polypeptide can be generated by removing one or more nucleotides from one end (for a terminal fragment) or both ends (for an internal fragment) of a nucleic acid which encodes the polypeptide. Expression of the mutagenized DNA produces polypeptide fragments. Digestion with "end-nibbling" endonucleases can thus generate DNA's which encode an array of fragments. DNA's which encode fragments of a protein can also be generated by random shearing, restriction digestion or a combination of the above-discussed methods.

Fragments can also be chemically synthesized using techniques known in the art such as conventional Merrifield solid phase f-Moc or t-Boc chemistry. For example, peptides of the present invention may be arbitrarily divided into fragments of desired length with no overlap of the fragments, or divided into overlapping fragments of a desired length.

Alteration of Nucleic Acids and Polypeptides: Random Methods

Amino acid sequence variants of a protein can be prepared by random mutagenesis of DNA which encodes a protein or a particular domain or region of a protein. Useful methods include PCR mutagenesis and saturation mutagenesis. A library of random amino acid sequence variants can also be generated by the synthesis of a set of degenerate oligonucleotide sequences. (Methods for screening proteins in a library of variants are elsewhere herein).

(A) PCR Mutagenesis

In PCR mutagenesis, reduced Taq polymerase fidelity is used to introduce random mutations into a cloned fragment of DNA (Leung et al., 1989, *Technique* 1:11-15). The DNA region to be mutagenized is amplified using the polymerase chain reaction (PCR) under conditions that reduce the fidelity of DNA synthesis by Taq DNA polymerase, e.g., by using a dGTP/dATP ratio of five and adding Mn²⁺ to the PCR reaction. The pool of amplified DNA fragments are inserted into appropriate cloning vectors to provide random mutant libraries.

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(B) Saturation Mutagenesis

Saturation mutagenesis allows for the rapid introduction of a large number of single base substitutions into cloned DNA fragments (Mayers et al., 1985, Science 229:242). This technique includes generation of mutations, e.g., by chemical treatment or irradiation of single-stranded DNA in vitro, and synthesis of a complimentary DNA strand. The mutation frequency can be modulated by modulating the severity of the treatment, and essentially all possible base substitutions can be obtained. Because this procedure does not involve a genetic selection for mutant fragments both neutral substitutions, as well as those that alter function, are obtained. The distribution of point mutations is not biased toward conserved sequence elements.

(C) Degenerate Oligonucleotides

A library of homologs can also be generated from a set of degenerate oligonucleotide sequences. Chemical synthesis of a degenerate sequences can be carried out in an automatic DNA synthesizer, and the synthetic genes then ligated into an appropriate expression vector. The synthesis of degenerate oligonucleotides is known in the art (see for example, Narang, SA (1983) Tetrahedron 39:3; Itakura et al. (1981) Recombinant DNA, Proc 3rd Cleveland Sympos. Macromolecules, ed. AG Walton, Amsterdam: Elsevier pp273-289; Itakura et al. (1984) Annu. Rev. Biochem. 53:323; Itakura et al. (1984) Science 198:1056; Ike et al. (1983) Nucleic Acid Res. 11:477. Such techniques have been employed in the directed evolution of other proteins (see, for example, Scott et al. (1990) Science 249:386-390; Roberts et al. (1992) PNAS 89:2429-2433; Devlin et al. (1990) Science 249: 404-406; Cwirla et al. (1990) PNAS 87: 6378-6382; as well as U.S. Patents Nos. 5,223,409, 5,198,346, and 5,096,815).

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Alteration of Nucleic Acids and Polypeptides: Methods for Directed Mutagenesis

Non-random or directed, mutagenesis techniques can be used to provide specific sequences or mutations in specific regions. These techniques can be used to create variants which include, e.g., deletions, insertions, or substitutions, of residues of the known amino acid sequence of a protein. The sites for mutation can be modified individually or in series, e.g., by (1) substituting first with conserved amino acids and then with more radical choices depending upon results achieved, (2) deleting the target residue, or (3) inserting residues of the same or a different class adjacent to the located site, or combinations of options 1-3.

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(A) Alanine Scanning Mutagenesis

Alanine scanning mutagenesis is a useful method for identification of certain residues or regions of the desired protein that are preferred locations or domains for mutagenesis. Cunningham and Wells (Science 244:1081-1085, 1989). In alanine scanning, a residue or group of target residues are identified (e.g., charged residues such as Arg, Asp, His, Lys, and Glu) and replaced by a neutral or negatively charged amino acid (most preferably alanine or polyalanine). Replacement of an amino acid can affect the interaction of the amino acids with the surrounding aqueous environment in or outside the cell. Those domains demonstrating functional sensitivity to the substitutions are then refined by introducing further or other variants at or for the sites of substitution. Thus, while the site for introducing an amino acid sequence variation is predetermined, the nature of the mutation per se need not be predetermined. For example, to optimize the performance of a mutation at a given site, alanine scanning or random mutagenesis may be conducted at the target codon or region and the expressed desired protein subunit variants are screened for the optimal combination of desired activity.

(B) Oligonucleotide-Mediated Mutagenesis

Oligonucleotide-mediated mutagenesis is a useful method for preparing substitution, deletion, and insertion variants of DNA, see, e.g., Adelman et al., (DNA 2:183, 1983). Briefly, the desired DNA is altered by hybridizing an oligonucleotide encoding a mutation to a DNA template, where the template is the single-stranded form of a plasmid or bacteriophage containing the unaltered or native DNA sequence of the desired protein. After hybridization, a DNA polymerase is used to synthesize an entire second complementary strand of the template that will thus incorporate the oligonucleotide primer, and will code for the selected alteration in the desired protein DNA. Generally, oligonucleotides of at least 25 nucleotides in length are used. An optimal oligonucleotide will have 12 to 15 nucleotides that are completely

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complementary to the template on either side of the nucleotide(s) coding for the mutation. This ensures that the oligonucleotide will hybridize properly to the single-stranded DNA template molecule. The oligonucleotides are readily synthesized using techniques known in the art such as that described by Crea et al. (*Proc. Natl. Acad. Sci.* USA, 75: 5765[1978]).

(C) Cassette Mutagenesis

Another method for preparing variants, cassette mutagenesis, is based on the technique described by Wells et al. (Gene, 34:315[1985]). The starting material is a plasmid (or other vector) which includes the protein subunit DNA to be mutated. The codon(s) in the protein subunit DNA to be mutated are identified. There must be a unique restriction endonuclease site on each side of the identified mutation site(s). If no such restriction sites exist, they may be generated using the above-described oligonucleotide-mediated mutagenesis method to introduce them at appropriate locations in the desired protein subunit DNA. After the restriction sites have been introduced into the plasmid, the plasmid is cut at these sites to linearize it. A double-stranded oligonucleotide encoding the sequence of the DNA between the restriction sites but containing the desired mutation(s) is synthesized using standard procedures. The two strands are synthesized separately and then hybridized together using standard techniques. This double-stranded oligonucleotide is referred to as the cassette. This cassette is designed to have 3' and 5' ends that are comparable with the ends of the linearized plasmid, such that it can be directly ligated to the plasmid. This plasmid now contains the mutated desired protein subunit DNA sequence.

25 (D) Combinatorial Mutagenesis

Combinatorial mutagenesis can also be used to generate mutants (Ladner et al., WO 88/06630). In this method, the amino acid sequences for a group of homologs or other related proteins are aligned, preferably to promote the highest homology possible. All of the amino acids which appear at a given position of the aligned sequences can be selected to create a degenerate set of combinatorial sequences. The variegated library of variants is generated by combinatorial mutagenesis at the nucleic acid level, and is encoded by a variegated gene library. For example, a mixture of synthetic oligonucleotides can be enzymatically ligated into gene sequences such that the degenerate set of potential sequences are expressible as individual peptides, or alternatively, as a set of larger fusion proteins containing the set of degenerate sequences.

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Other Modifications of H. pylori Nucleic Acids and Polypeptides

It is possible to modify the structure of an *H. pylori* polypeptide for such purposes as increasing solubility, enhancing stability (e.g., shelf life *ex vivo* and resistance to proteolytic degradation *in vivo*). A modified *H. pylori* protein or peptide can be produced in which the amino acid sequence has been altered, such as by amino acid substitution, deletion, or addition as described herein.

An *H. pylori* peptide can also be modified by substitution of cysteine residues preferably with alanine, serine, threonine, leucine or glutamic acid residues to minimize dimerization via disulfide linkages. In addition, amino acid side chains of fragments of the protein of the invention can be chemically modified. Another modification is cyclization of the peptide.

In order to enhance stability and/or reactivity, an *H. pylori* polypeptide can be modified to incorporate one or more polymorphisms in the amino acid sequence of the protein resulting from any natural allelic variation. Additionally, D-amino acids, non-natural amino acids, or non-amino acid analogs can be substituted or added to produce a modified protein within the scope of this invention. Furthermore, an *H. pylori* polypeptide can be modified using polyethylene glycol (PEG) according to the method of A. Sehon and co-workers (Wie et al., supra) to produce a protein conjugated with PEG. In addition, PEG can be added during chemical synthesis of the protein. Other modifications of *H. pylori* proteins include reduction/alkylation (Tarr, *Methods of Protein Microcharacterization*, J. E. Silver ed., Humana Press, Clifton NJ 155-194 (1986)); acylation (Tarr, supra); chemical coupling to an appropriate carrier (Mishell and Shiigi, eds, *Selected Methods in Cellular Immunology*, WH Freeman, San Francisco, CA (1980), U.S. Patent 4,939,239; or mild formalin treatment (Marsh, (1971) *Int. Arch. of Allergy and Appl. Immunol.*, 41: 199 - 215).

To facilitate purification and potentially increase solubility of an *H. pylori* protein or peptide, it is possible to add an amino acid fusion moiety to the peptide backbone. For example, hexa-histidine can be added to the protein for purification by immobilized metal ion affinity chromatography (Hochuli, E. et al., (1988) *Bio/Technology*, 6: 1321 - 1325). In addition, to facilitate isolation of peptides free of irrelevant sequences, specific endoprotease cleavage sites can be introduced between the sequences of the fusion moiety and the peptide.

To potentially aid proper antigen processing of epitopes within an *H. pylori* polypeptide, canonical protease sensitive sites can be engineered between regions, each comprising at least one epitope via recombinant or synthetic methods. For example, charged amino acid pairs, such as KK or RR, can be introduced between regions within a protein or fragment during recombinant construction thereof. The resulting peptide

can be rendered sensitive to cleavage by cathepsin and/or other trypsin-like enzymes which would generate portions of the protein containing one or more epitopes. In addition, such charged amino acid residues can result in an increase in the solubility of the peptide.

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Primary Methods for Screening Polypeptides and Analogs

Various techniques are known in the art for screening generated mutant gene products. Techniques for screening large gene libraries often include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of vectors, and expressing the genes under conditions in which detection of a desired activity, e.g., in this case, binding to *H. pylori* polypeptide or an interacting protein, facilitates relatively easy isolation of the vector encoding the gene whose product was detected. Each of the techniques described below is amenable to high through-put analysis for screening large numbers of sequences created, e.g., by random mutagenesis techniques.

(A) Two Hybrid Systems

Two hybrid assays such as the system described above (as with the other screening methods described herein), can be used to identify polypeptides, e.g., fragments or analogs of a naturally-occurring *H. pylori* polypeptide, e.g., of cellular proteins, or of randomly generated polypeptides which bind to an *H. pylori* protein. (The *H. pylori* domain is used as the bait protein and the library of variants are expressed as fish fusion proteins.) In an analogous fashion, a two hybrid assay (as with the other screening methods described herein), can be used to find polypeptides which bind a *H. pylori* polypeptide.

(B) Display Libraries

In one approach to screening assays, the candidate peptides are displayed on the surface of a cell or viral particle, and the ability of particular cells or viral particles to bind an appropriate receptor protein via the displayed product is detected in a "panning assay". For example, the gene library can be cloned into the gene for a surface membrane protein of a bacterial cell, and the resulting fusion protein detected by panning (Ladner et al., WO 88/06630; Fuchs et al. (1991) *Bio/Technology* 9:1370-1371; and Goward et al. (1992) *TIBS* 18:136-140). In a similar fashion, a detectably labeled ligand can be used to score for potentially functional peptide homologs. Fluorescently labeled ligands, e.g., receptors, can be used to detect homologs which retain ligand-binding activity. The use of fluorescently labeled ligands, allows cells to be visually

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inspected and separated under a fluorescence microscope, or, where the morphology of the cell permits, to be separated by a fluorescence-activated cell sorter.

A gene library can be expressed as a fusion protein on the surface of a viral particle. For instance, in the filamentous phage system, foreign peptide sequences can be expressed on the surface of infectious phage, thereby conferring two significant benefits. First, since these phage can be applied to affinity matrices at concentrations well over 10¹³ phage per milliliter, a large number of phage can be screened at one time. Second, since each infectious phage displays a gene product on its surface, if a particular phage is recovered from an affinity matrix in low yield, the phage can be amplified by another round of infection. The group of almost identical E. coli filamentous phages M13, fd., and fl are most often used in phage display libraries. Either of the phage gIII or gVIII coat proteins can be used to generate fusion proteins without disrupting the ultimate packaging of the viral particle. Foreign epitopes can be expressed at the NH2terminal end of pIII and phage bearing such epitopes recovered from a large excess of phage lacking this epitope (Ladner et al. PCT publication WO 90/02909; Garrard et al., PCT publication WO 92/09690; Marks et al. (1992) J. Biol. Chem. 267:16007-16010; Griffiths et al. (1993) EMBO J 12:725-734; Clackson et al. (1991) Nature 352:624-628; and Barbas et al. (1992) PNAS 89:4457-4461).

A common approach uses the maltose receptor of E. coli (the outer membrane protein, LamB) as a peptide fusion partner (Charbit et al. (1986) EMBO 5, 3029-3037). 20 Oligonucleotides have been inserted into plasmids encoding the LamB gene to produce peptides fused into one of the extracellular loops of the protein. These peptides are available for binding to ligands, e.g., to antibodies, and can elicit an immune response when the cells are administered to animals. Other cell surface proteins, e.g., OmpA (Schorr et al. (1991) Vaccines 91, pp. 387-392), PhoE (Agterberg, et al. (1990) Gene 88, 25 37-45), and PAL (Fuchs et al. (1991) Bio/Tech 9, 1369-1372), as well as large bacterial surface structures have served as vehicles for peptide display. Peptides can be fused to pilin, a protein which polymerizes to form the pilus-a conduit for interbacterial exchange of genetic information (Thiry et al. (1989) Appl. Environ. Microbiol. 55, 984-993). Because of its role in interacting with other cells, the pilus provides a useful support for 30 the presentation of peptides to the extracellular environment. Another large surface structure used for peptide display is the bacterial motive organ, the flagellum. Fusion of peptides to the subunit protein flagellin offers a dense array of many peptide copies on the host cells (Kuwajima et al. (1988) Bio/Tech. 6, 1080-1083). Surface proteins of other bacterial species have also served as peptide fusion partners. Examples include the 35 Staphylococcus protein A and the outer membrane IgA protease of Neisseria (Hansson

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et al. (1992) J. Bacteriol. 174, 4239-4245 and Klauser et al. (1990) EMBO J. 9, 1991-1999).

In the filamentous phage systems and the LamB system described above, the physical link between the peptide and its encoding DNA occurs by the containment of the DNA within a particle (cell or phage) that carries the peptide on its surface. Capturing the peptide captures the particle and the DNA within. An alternative scheme uses the DNA-binding protein LacI to form a link between peptide and DNA (Cull et al. (1992) PNAS USA 89:1865-1869). This system uses a plasmid containing the LacI gene with an oligonucleotide cloning site at its 3'-end. Under the controlled induction by arabinose, a LacI-peptide fusion protein is produced. This fusion retains the natural ability of LacI to bind to a short DNA sequence known as LacO operator (LacO). By installing two copies of LacO on the expression plasmid, the LacI-peptide fusion binds tightly to the plasmid that encoded it. Because the plasmids in each cell contain only a single oligonucleotide sequence and each cell expresses only a single peptide sequence, the peptides become specifically and stably associated with the DNA sequence that directed its synthesis. The cells of the library are gently lysed and the peptide-DNA complexes are exposed to a matrix of immobilized receptor to recover the complexes containing active peptides. The associated plasmid DNA is then reintroduced into cells for amplification and DNA sequencing to determine the identity of the peptide ligands. As a demonstration of the practical utility of the method, a large random library of dodecapeptides was made and selected on a monoclonal antibody raised against the opioid peptide dynorphin B. A cohort of peptides was recovered, all related by a consensus sequence corresponding to a six-residue portion of dynorphin B. (Cull et al. (1992) Proc. Natl. Acad. Sci. U.S.A. 89-1869)

This scheme, sometimes referred to as peptides-on-plasmids, differs in two important ways from the phage display methods. First, the peptides are attached to the C-terminus of the fusion protein, resulting in the display of the library members as peptides having free carboxy termini. Both of the filamentous phage coat proteins, pIII and pVIII, are anchored to the phage through their C-termini, and the guest peptides are placed into the outward-extending N-terminal domains. In some designs, the phage-displayed peptides are presented right at the amino terminus of the fusion protein. (Cwirla, et al. (1990) *Proc. Natl. Acad. Sci. U.S.A.* 87, 6378-6382) A second difference is the set of biological biases affecting the population of peptides actually present in the libraries. The LacI fusion molecules are confined to the cytoplasm of the host cells. The phage coat fusions are exposed briefly to the cytoplasm during translation but are rapidly secreted through the inner membrane into the periplasmic compartment, remaining anchored in the membrane by their C-terminal hydrophobic domains, with the

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N-termini, containing the peptides, protruding into the periplasm while awaiting assembly into phage particles. The peptides in the LacI and phage libraries may differ significantly as a result of their exposure to different proteolytic activities. The phage coat proteins require transport across the inner membrane and signal peptidase processing as a prelude to incorporation into phage. Certain peptides exert a deleterious effect on these processes and are underrepresented in the libraries (Gallop et al. (1994) J. Med. Chem. 37(9):1233-1251). These particular biases are not a factor in the LacI display system.

The number of small peptides available in recombinant random libraries is enormous. Libraries of 10^7 - 10^9 independent clones are routinely prepared. Libraries as large as 10^{11} recombinants have been created, but this size approaches the practical limit for clone libraries. This limitation in library size occurs at the step of transforming the DNA containing randomized segments into the host bacterial cells. To circumvent this limitation, an *in vitro* system based on the display of nascent peptides in polysome complexes has recently been developed. This display library method has the potential of producing libraries 3-6 orders of magnitude larger than the currently available phage/phagemid or plasmid libraries. Furthermore, the construction of the libraries, expression of the peptides, and screening, is done in an entirely cell-free format.

In one application of this method (Gallop et al. (1994) J. Med. Chem. 37(9):1233-1251), a molecular DNA library encoding 1012 decapeptides was 20 constructed and the library expressed in an E. coli S30 in vitro coupled transcription/translation system. Conditions were chosen to stall the ribosomes on the mRNA, causing the accumulation of a substantial proportion of the RNA in polysomes and yielding complexes containing nascent peptides still linked to their encoding RNA. The polysomes are sufficiently robust to be affinity purified on immobilized receptors in 25 much the same way as the more conventional recombinant peptide display libraries are screened. RNA from the bound complexes is recovered, converted to cDNA, and amplified by PCR to produce a template for the next round of synthesis and screening. The polysome display method can be coupled to the phage display system. Following several rounds of screening, cDNA from the enriched pool of polysomes was cloned into 30 a phagemid vector. This vector serves as both a peptide expression vector, displaying peptides fused to the coat proteins, and as a DNA sequencing vector for peptide identification. By expressing the polysome-derived peptides on phage, one can either continue the affinity selection procedure in this format or assay the peptides on individual clones for binding activity in a phage ELISA, or for binding specificity in a 35 completion phage ELISA (Barret, et al. (1992) Anal. Biochem 204,357-364). To

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identify the sequences of the active peptides one sequences the DNA produced by the phagemid host.

Secondary Screening of Polypeptides and Analogs

The high through-put assays described above can be followed by secondary screens in order to identify further biological activities which will, e.g., allow one skilled in the art to differentiate agonists from antagonists. The type of a secondary screen used will depend on the desired activity that needs to be tested. For example, an assay can be developed in which the ability to inhibit an interaction between a protein of interest and its respective ligand can be used to identify antagonists from a group of peptide fragments isolated though one of the primary screens described above.

Therefore, methods for generating fragments and analogs and testing them for activity are known in the art. Once the core sequence of interest is identified, it is routine for one skilled in the art to obtain analogs and fragments.

Peptide Mimetics of H. pylori Polypeptides

The invention also provides for reduction of the protein binding domains of the subject *H. pylori* polypeptides to generate mimetics, e.g. peptide or non-peptide agents. The peptide mimetics are able to disrupt binding of a polypeptide to its counter ligand, e.g., in the case of an *H. pylori* polypeptide binding to a naturally occurring ligand. The critical residues of a subject *H. pylori* polypeptide which are involved in molecular recognition of a polypeptide can be determined and used to generate *H. pylori*-derived peptidomimetics which competitively or noncompetitively inhibit binding of the *H. pylori* polypeptide with an interacting polypeptide (see, for example, European patent applications EP-412,762A and EP-B31,080A).

For example, scanning mutagenesis can be used to map the amino acid residues of a particular *H. pylori* polypeptide involved in binding an interacting polypeptide, peptidomimetic compounds (e.g. diazepine or isoquinoline derivatives) can be generated which mimic those residues in binding to an interacting polypeptide, and which therefore can inhibit binding of an *H. pylori* polypeptide to an interacting polypeptide and thereby interfere with the function of *H. pylori* polypeptide. For instance, non-hydrolyzable peptide analogs of such residues can be generated using benzodiazepine (e.g., see Freidinger et al. in *Peptides: Chemistry and Biology*, G.R. Marshall ed., ESCOM Publisher: Leiden, Netherlands, 1988), azepine (e.g., see Huffman et al. in *Peptides: Chemistry and Biology*, G.R. Marshall ed., ESCOM Publisher: Leiden, Netherlands, 1988), substituted gama lactam rings (Garvey et al. in *Peptides: Chemistry and Biology*, G.R. Marshall ed., ESCOM Publisher: Leiden, Netherlands, 1988), keto-

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methylene pseudopeptides (Ewenson et al. (1986) *J Med Chem* 29:295; and Ewenson et al. in *Peptides: Structure and Function* (Proceedings of the 9th American Peptide Symposium) Pierce Chemical Co. Rockland, IL, 1985), β-turn dipeptide cores (Nagai et al. (1985) *Tetrahedron Lett* 26:647; and Sato et al. (1986) *J Chem Soc Perkin Trans* 1:1231), and β-aminoalcohols (Gordon et al. (1985) *Biochem Biophys Res Commun* 134:71).

VI. Vaccine Formulations for H. pylori Nucleic Acids and Polypeptides

This invention also features vaccine compositions or formulations (used interchangeably herein) for protection against infection by H. pylori or for treatment of H. pylori infection. As used herein, the term "treatment of H. pylori infection" refers to therapeutic treatment of an existing or established H. pylori infection. The terms "protection against H. pylori infection" or "prophylactic treatment" refer to the use of H. pylori vaccine formulation for reducing the risk of or preventing an infection in a subject at risk for H. pylori infection. In one embodiment, the vaccine compositions contain one or more immunogenic components, such as a surface protein, from H. pylori, or portion thereof, and a pharmaceutically acceptable carrier. For example, in one embodiment, the vaccine formulations of the invention contain at least one or combination of H. pylori polypeptides or fragments thereof, from same or different H. pylori antigens. Nucleic acids and H. pylori polypeptides for use in the vaccine formulations of the invention include the nucleic acids and polypeptides set forth in the Sequence Listing, preferably those H. pylori nucleic acids that encode surface proteins and surface proteins or fragments thereof. For example, a preferred nucleic acid and H. pylori polypeptide for use in a vaccine composition of the invention is selected from the group of nucleic acids which encode cell envelope proteins and H. pylori cell envelope proteins as set forth in Table 1. However, any nucleic acid encoding an immunogenic H. pylori protein and H. pylori polypetide, or portion thereof, can be used in the present invention. These vaccines have therapeutic and/or prophylactic utilities.

One aspect of the invention provides a vaccine composition for protection against infection by *H. pylori* which contains at least one immunogenic fragment of an *H. pylori* protein and a pharmaceutically acceptable carrier. Preferred fragments include peptides of at least about 10 amino acid residues in length, preferably about 10-20 amino acid residues in length, and more preferably about 12-16 amino acid residues in length.

Immunogenic components of the invention can be obtained, for example, by screening polypeptides recombinantly produced from the corresponding fragment of the nucleic acid encoding the full-length *H. pylori* protein. In addition, fragments can be

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chemically synthesized using techniques known in the art such as conventional Merrifield solid phase f-Moc or t-Boc chemistry.

In one embodiment, immunogenic components are identified by the ability of the peptide to stimulate T cells. Peptides which stimulate T cells, as determined by, for example, T cell proliferation or cytokine secretion are defined herein as comprising at least one T cell epitope. T cell epitopes are believed to be involved in initiation and perpetuation of the immune response to the protein allergen which is responsible for the clinical symptoms of allergy. These T cell epitopes are thought to trigger early events at the level of the T helper cell by binding to an appropriate HLA molecule on the surface of an antigen presenting cell, thereby stimulating the T cell subpopulation with the relevant T cell receptor for the epitope. These events lead to T cell proliferation, lymphokine secretion, local inflammatory reactions, recruitment of additional immune cells to the site of antigen/T cell interaction, and activation of the B cell cascade, leading to the production of antibodies. A T cell epitope is the basic element, or smallest unit of recognition by a T cell receptor, where the epitope comprises amino acids essential to receptor recognition (e.g., approximately 6 or 7 amino acid residues). Amino acid sequences which mimic those of the T cell epitopes are within the scope of this invention.

In another embodiment, immunogenic components of the invention are identified through genomic vaccination. The basic protocol is based on the idea that expression libraries consisting of all or parts of a pathogen genome, e.g., an *H. pylori* genome, can confer protection when used to genetically immunize a host. This expression library immunization (ELI) is analogous to expression cloning and involves reducing a genomic expression library of a pathogen, e.g., *H. pylori*, into plasmids that can act as genetic vaccines. The plasmids can also be designed to encode genetic adjuvants which can dramatically stimulate the humoral response. These genetic adjuvants can be introduced at remote sites and act as well extracelluraly as intracellularly.

This is a new approach to vaccine production that has many of the advantages of live/attenuated pathogens but no risk of infection. An expression library of pathogen DNA is used to immunize a host thereby producing the effects of antigen presentation of a live vaccine without the risk. For example, in the present invention, random fragments from the *H. pylori* genome or from cosmid or plasmid clones, as well as PCR products from genes identified by genomic sequencing, can be used to immunize a host. The feasibility of this approach has been demonstrated with *Mycoplasma pulmonis* (Barry et al., *Nature* 377:632-635, 1995), where even partial expression libraries of *Mycoplasma pulmonis*, a natural pathogen in rodents, provided protection against challenge from the pathogen.

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ELI is a technique that allows for production of a non-infectious multipartite vaccine, even when little is known about pathogen's biology, because ELI uses the immune system to screen candidate genes. Once isolated, these genes can be used as genetic vaccines or for development of recombinant protein vaccines. Thus, ELI allows for production of vaccines in a systematic, largely mechanized fashion.

Screening immunogenic components can be accomplished using one or more of several different assays. For example, *in vitro*, peptide T cell stimulatory activity is assayed by contacting a peptide known or suspected of being immunogenic with an antigen presenting cell which presents appropriate MHC molecules in a T cell culture. Presentation of an immunogenic *H. pylori* peptide in association with appropriate MHC molecules to T cells in conjunction with the necessary costimulation has the effect of transmitting a signal to the T cell that induces the production of increased levels of cytokines, particularly of interleukin-2 and interleukin-4. The culture supernatant can be obtained and assayed for interleukin-2 or other known cytokines. For example, any one of several conventional assays for interleukin-2 can be employed, such as the assay described in *Proc. Natl. Acad. Sci USA*, 86: 1333 (1989) the pertinent portions of which are incorporated herein by reference. A kit for an assay for the production of interferon is also available from Genzyme Corporation (Cambridge, MA).

Alternatively, a common assay for T cell proliferation entails measuring tritiated thymidine incorporation. The proliferation of T cells can be measured *in vitro* by determining the amount of ³H-labeled thymidine incorporated into the replicating DNA of cultured cells. Therefore, the rate of DNA synthesis and, in turn, the rate of cell division can be quantified.

Vaccine compositions or formulations of the invention containing one or more immunogenic components (e.g., *H. pylori* polypeptide or fragment thereof or nucleic acid encoding an *H. pylori* polypeptide or fragment thereof) preferably include a pharmaceutically acceptable carrier. The term "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. Suitable pharmaceutically acceptable carriers include, for example, one or more of water, saline, phosphate buffered saline, dextrose, glycerol, ethanol and the like, as well as combinations thereof. Pharmaceutically acceptable carriers may further comprise minor amounts of auxiliary substances such as wetting or emulsifying agents, preservatives or buffers, which enhance the shelf life or effectiveness of the *H. pylori* nucleic acid or polypeptide. For vaccine formulations of the invention containing *H. pylori* polypeptides, the polypeptide is preferably coadministered with a suitable adjuvant and/or a delivery system described herein.

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It will be apparent to those of skill in the art that the therapeutically effective amount of DNA or protein of this invention will depend, *inter alia*, upon the administration schedule, the unit dose of an *H. pylori* nucleic acid or polypeptide administered, whether the protein or nucleic acid is administered in combination with other therapeutic agents, the immune status and health of the patient, and the therapeutic activity of the particular protein or nucleic acid.

Vaccine formulations are conventionally administered parenterally, e.g., by injection, either subcutaneously or intramuscularly. Methods for intramuscular immunization are described by Wolff et al. (1990) Science 247: 1465-1468 and by Sedegah et al. (1994) Immunology 91: 9866-9870. Other modes of administration include oral and pulmonary formulations, suppositories, and transdermal applications. Oral immunization is preferred over parenteral methods for inducing protection against infection by H. pylori. Czinn et. al. (1993) Vaccine 11: 637-642. Oral formulations include such normally employed excipients as, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, and the like.

In one embodiment, the vaccine formulation includes, as a pharmaceutically acceptable carrier, an adjuvant. Examples of the suitable adjuvants for use in the vaccine formulations of the invention include, but are not limited, to aluminum hydroxide; N-acetyl-muramyl--L-threonyl-D-isoglutamine (thr-MDP); N-acetyl-nor-20 muramyl-L-alanyl-D-isoglutamine (CGP 11637, referred to as nor-MDP); Nacetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3hydroxyphos-phoryloxy)-ethylamine (CGP 19835A, referred to a MTP-PE); RIBI, which contains three components from bacteria; monophosphoryl lipid A; trehalose dimycoloate; cell wall skeleton (MPL + TDM + CWS) in a 2% squalene/Tween 80 25 emulsion; and cholera toxin. Others which may be used are non-toxic derivatives of cholera toxin, including its B subunit, and/or conjugates or genetically engineered fusions of the H. pylori polypeptide with cholera toxin or its B subunit, procholeragenoid, fungal polysaccharides, including schizophyllan, muramyl dipeptide, muramyl dipeptide derivatives, phorbol esters, labile toxin of E. coli, non-H. pylori 30 bacterial lysates, block polymers or saponins.

In another embodiment, the vaccine formulation includes, as a pharmaceutically acceptable carrier, a delivery system. Suitable delivery systems for use in the vaccine formulations of the invention include biodegradable microcapsules or immunostimulating complexes (ISCOMs), cochleates, or liposomes, genetically engineered attenuated live vectors such as viruses or bacteria, and recombinant (chimeric) virus-like

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particles, e.g., bluetongue. In another embodiment of the invention, the vaccine formulation includes both a delivery system and an adjuvant.

Delivery systems in humans may include enteric release capsules protecting the antigen from the acidic environment of the stomach, and including *H. pylori* polypeptide in an insoluble form as fusion proteins. Suitable carriers for the vaccines of the invention are enteric coated capsules and polylactide-glycolide microspheres. Suitable diluents are 0.2 N NaHCO3 and/or saline.

Vaccines of the invention can be administered as a primary prophylactic agent in adults or in children, as a secondary prevention, after successful eradication of H. pylori in an infected host, or as a therapeutic agent in the aim to induce an immune response in a susceptible host to prevent infection by H. pylori. The vaccines of the invention are administered in amounts readily determined by persons of ordinary skill in the art. Thus, for adults a suitable dosage will be in the range of 10 μ g to 10 g, preferably 10 μ g to 100 mg, for example 50 μ g to 50 mg. A suitable dosage for adults will also be in the range of 5 μ g to 500 mg. Similar dosage ranges will be applicable for children.

The amount of adjuvant employed will depend on the type of adjuvant used. For example, when the mucosal adjuvant is cholera toxin, it is suitably used in an amount of 5 μ g to 50 μ g, for example 10 μ g to 35 μ g. When used in the form of microcapsules, the amount used will depend on the amount employed in the matrix of the microcapsule to achieve the desired dosage. The determination of this amount is within the skill of a person of ordinary skill in the art.

Those skilled in the art will recognize that the optimal dose may be more or less depending upon the patient's body weight, disease, the route of administration, and other factors. Those skilled in the art will also recognize that appropriate dosage levels can be obtained based on results with known oral vaccines such as, for example, a vaccine based on an *E. coli* lysate (6 mg dose daily up to total of 540 mg) and with an enterotoxigenic *E. coli* purified antigen (4 doses of 1 mg) (Schulman et al., *J. Urol.* 150:917-921 (1993)); Boedecker et al., *American Gastroenterological Assoc.* 999:A-222 (1993)). The number of doses will depend upon the disease, the formulation, and efficacy data from clinical trials. Without intending any limitation as to the course of treatment, the treatment can be administered over 3 to 8 doses for a primary immunization schedule over 1 month (Boedeker, *American Gastroenterological Assoc.* 888:A-222 (1993)).

In a preferred embodiment, a vaccine composition of the invention can be based on a killed whole *E. coli* preparation with an immunogenic fragment of an *H. pylori* protein of the invention expressed on its surface or it can be based on an *E. coli* lysate, wherein the killed *E. coli* acts as a carrier or an adjuvant.

It will be apparent to those skilled in the art that some of the vaccine compositions of the invention are useful only for preventing *H. pylori* infection, some are useful only for treating *H. pylori* infection, and some are useful for both preventing and treating *H. pylori* infection. In a preferred embodiment, the vaccine composition of the invention provides protection against *H. pylori* infection by stimulating humoral and/or cell-mediated immunity against *H. pylori*. It should be understood that amelioration of any of the symptoms of *H. pylori* infection is a desirable clinical goal, including a lessening of the dosage of medication used to treat *H. pylori*-caused disease, or an increase in the production of antibodies in the serum or mucous of patients.

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VII. Antibodies Reactive With H. pylori Polypeptides

The invention also includes antibodies specifically reactive with the subject *H. pylori* polypeptide. Anti-protein/anti-peptide antisera or monoclonal antibodies can be made by standard protocols (See, for example, *Antibodies: A Laboratory Manual* ed. by Harlow and Lane (Cold Spring Harbor Press: 1988)). A mammal such as a mouse, a hamster or rabbit can be immunized with an immunogenic form of the peptide. Techniques for conferring immunogenicity on a protein or peptide include conjugation to carriers or other techniques well known in the art. An immunogenic portion of the subject *H. pylori* polypeptide can be administered in the presence of adjuvant. The progress of immunization can be monitored by detection of antibody titers in plasma or serum. Standard ELISA or other immunoassays can be used with the immunogen as antigen to assess the levels of antibodies.

In a preferred embodiment, the subject antibodies are immunospecific for antigenic determinants of the *H. pylori* polypeptides of the invention, e.g. antigenic determinants of a polypeptide of the invention contained in the Sequence Listing, or a closely related human or non-human mammalian homolog (e.g., 90% homologous, more preferably at least 95% homologous). In yet a further preferred embodiment of the invention, the anti-*H. pylori* antibodies do not substantially cross react (i.e., react specifically) with a protein which is for example, less than 80% percent homologous to a sequence of the invention contained in the Sequence Listing. By "not substantially cross react", it is meant that the antibody has a binding affinity for a non-homologous protein which is less than 10 percent, more preferably less than 5 percent, and even more preferably less than 1 percent, of the binding affinity for a protein of the invention contained in the Sequence Listing. In a most preferred embodiment, there is no crossreactivity between bacterial and mammalian antigens.

The term antibody as used herein is intended to include fragments thereof which are also specifically reactive with *H. pylori* polypeptides. Antibodies can be fragmented

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using conventional techniques and the fragments screened for utility in the same manner as described above for whole antibodies. For example, F(ab')₂ fragments can be generated by treating antibody with pepsin. The resulting F(ab')₂ fragment can be treated to reduce disulfide bridges to produce Fab' fragments. The antibody of the invention is further intended to include bispecific and chimeric molecules having an anti-H. pylori portion.

Both monoclonal and polyclonal antibodies (Ab) directed against *H. pylori* polypeptides or *H. pylori* polypeptide variants, and antibody fragments such as Fab' and F(ab')2, can be used to block the action of *H. pylori* polypeptide and allow the study of the role of a particular *H. pylori* polypeptide of the invention in aberrant or unwanted intracellular signaling, as well as the normal cellular function of the *H. pylori* and by microinjection of anti-*H. pylori* polypeptide antibodies of the present invention.

Antibodies which specifically bind *H. pylori* epitopes can also be used in immunohistochemical staining of tissue samples in order to evaluate the abundance and pattern of expression of *H. pylori* antigens. Anti *H. pylori* polypeptide antibodies can be used diagnostically in immuno-precipitation and immuno-blotting to detect and evaluate *H. pylori* levels in tissue or bodily fluid as part of a clinical testing procedure. Likewise, the ability to monitor *H. pylori* polypeptide levels in an individual can allow determination of the efficacy of a given treatment regimen for an individual afflicted with such a disorder. The level of an *H. pylori* polypeptide can be measured in cells found in bodily fluid, such as in urine samples or can be measured in tissue, such as produced by gastric biopsy. Diagnostic assays using anti-*H. pylori* antibodies can include, for example, immunoassays designed to aid in early diagnosis of *H. pylori* infections. The present invention can also be used as a method of detecting antibodies contained in samples from individuals infected by this bacterium using specific *H. pylori* antigens.

Another application of anti-*H. pylori* polypeptide antibodies of the invention is in the immunological screening of cDNA libraries constructed in expression vectors such as $\lambda gt11$, $\lambda gt18-23$, λZAP , and $\lambda ORF8$. Messenger libraries of this type, having coding sequences inserted in the correct reading frame and orientation, can produce fusion proteins. For instance, $\lambda gt11$ will produce fusion proteins whose amino termini consist of β -galactosidase amino acid sequences and whose carboxy termini consist of a foreign polypeptide. Antigenic epitopes of a subject *H. pylori* polypeptide can then be detected with antibodies, as, for example, reacting nitrocellulose filters lifted from infected plates with anti-*H. pylori* polypeptide antibodies. Phage, scored by this assay, can then be isolated from the infected plate. Thus, the presence of *H. pylori* gene

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homologs can be detected and cloned from other species, and alternate isoforms (including splicing variants) can be detected and cloned.

VIII. Kits Containing Nucleic Acids, Polypeptides or Antibodies of the Invention

The nucleic acid, polypeptides and antibodies of the invention can be combined with other reagents and articles to form kits. Kits for diagnostic purposes typically comprise the nucleic acid, polypeptides or antibodies in vials or other suitable vessels. Kits typically comprise other reagents for performing hybridization reactions, polymerase chain reactions (PCR), or for reconstitution of lyophilized components, such as aqueous media, salts, buffers, and the like. Kits may also comprise reagents for sample processing such as detergents, chaotropic salts and the like. Kits may also comprise immobilization means such as particles, supports, wells, dipsticks and the like. Kits may also comprise labeling means such as dyes, developing reagents, radioisotopes, fluorescent agents, luminescent or chemiluminescent agents, enzymes, intercalating agents and the like. With the nucleic acid and amino acid sequence information provided herein, individuals skilled in art can readily assemble kits to serve their particular purpose. Kits further can include instructions for use.

IX. Drug Screening Assays Using H. pylori Polypeptides

By making available purified and recombinant *H. pylori* polypeptides, the present invention provides assays which can be used to screen for drugs which are either agonists or antagonists of the normal cellular function, in this case, of the subject *H. pylori* polypeptides, or of their role in intracellular signaling. Such inhibitors or potentiators may be useful as new therapeutic agents to combat *H. pylori* infections in humans. A variety of assay formats will suffice and, in light of the present inventions, will be comprehended by the skilled artisan.

In many drug screening programs which test libraries of compounds and natural extracts, high throughput assays are desirable in order to maximize the number of compounds surveyed in a given period of time. Assays which are performed in cell-free systems, such as may be derived with purified or semi-purified proteins, are often preferred as "primary" screens in that they can be generated to permit rapid development and relatively easy detection of an alteration in a molecular target which is mediated by a test compound. Moreover, the effects of cellular toxicity and/or bioavailability of the test compound can be generally ignored in the *in vitro* system, the assay instead being focused primarily on the effect of the drug on the molecular target as may be manifest in an alteration of binding affinity with other proteins or change in enzymatic properties of the molecular target. Accordingly, in an exemplary screening assay of the present

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invention, the compound of interest is contacted with an isolated and purified *H. pylori* polypeptide.

Screening assays can be constructed *in vitro* with a purified *H. pylori* polypeptide or fragment thereof, such as an *H. pylori* polypeptide having enzymatic activity, such that the activity of the polypeptide produces a detectable reaction product. The efficacy of the compound can be assessed by generating dose response curves from data obtained using various concentrations of the test compound. Moreover, a control assay can also be performed to provide a baseline for comparison. Suitable products include those with distinctive absorption, fluorescence, or chemi-luminescence properties, for example, because detection may be easily automated. A variety of synthetic or naturally occurring compounds can be tested in the assay to identify those which inhibit or potentiate the activity of the *H. pylori* polypeptide. Some of these active compounds may directly, or with chemical alterations to promote membrane permeability or solubility, also inhibit or potentiate the same activity (e.g., enzymatic activity) in whole, live *H. pylori* cells.

This invention is further illustrated by the following examples which should not be construed as limiting. The contents of all references and published patent applications cited throughout this application are hereby incorporated by reference.

EXEMPLIFICATION

I. Cloning and Sequencing of H. pylori DNA

H. pylori chromosomal DNA was isolated according to a basic DNA protocol outlined in Schleif R.F. and Wensink P.C., Practical Methods in Molecular Biology, p.98, Springer-Verlag, NY., 1981, with minor modifications. Briefly, cells were pelleted, resuspended in TE (10 mM Tris, 1 mM EDTA, pH 7.6) and GES lysis buffer (5.1 M guanidium thiocyanate, 0.1 M EDTA, pH 8.0, 0.5% N-laurylsarcosine) was added. Suspension was chilled and ammonium acetate (NH₄Ac) was added to final concentration of 2.0 M. DNA was extracted, first with chloroform, then with phenol-chloroform, and reextracted with chloroform. DNA was precipitated with isopropanol, washed twice with 70% EtOH, dried and resuspended in TE.

Following isolation whole genomic *H. pylori* DNA was nebulized (Bodenteich et al., *Automated DNA Sequencing and Analysis* (J.C. Venter, ed.), Academic Press, 1994) to a median size of 2000 bp. After nebulization, the DNA was concentrated and separated on a standard 1% agarose gel. Several fractions, corresponding to

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approximate sizes 900-1300 bp, 1300-1700 bp, 1700-2200 bp, 2200-2700 bp, were excised from the gel and purified by the GeneClean procedure (Bio101, Inc.).

The purified DNA fragments were then blunt-ended using T4 DNA polymerase. The healed DNA was then ligated to unique BstXI-linker adapters in 100-1000 fold molar excess. These linkers are complimentary to the BstXI-cut pMPX vectors, while the overhang is not self-complimentary. Therefore, the linkers will not concatemerize nor will the cut-vector religate itself easily. The linker-adopted inserts were separated from the unincorporated linkers on a 1% agarose gel and purified using GeneClean. The linker-adopted inserts were then ligated to each of the 20 pMPX vectors to construct a series of "shotgun" subclone libraries. The vectors contain an out-of-frame lacZ gene at the cloning site which becomes in-frame in the event that an adapter-dimer is cloned, allowing these to be avoided by their blue-color.

All subsequent steps were based on the multiplex DNA sequencing protocols outlined in Church G.M. and Kieffer-Higgins S., Science 240:185-188, 1988. Only major modifications to the protocols are highlighted. Briefly, each of the 20 vectors was then transformed into DH5α competent cells (Gibco/BRL, DH5α transformation protocol). The libraries were assessed by plating onto antibiotic plates containing ampicillin, methicillin and IPTG/Xgal. The plates were incubated overnight at 37°C. Successful transformants were then used for plating of clones and pooling into the multiplex pools. The clones were picked and pooled into 40 ml growth medium cultures. The cultures were grown overnight at 37°C. DNA was purified using the Qiagen Midi-prep kits and Tip-100 columns (Qiagen, Inc.). In this manner, 100 μg of DNA was obtained per pool. Fifteen 96-well plates of DNA were generated to obtain a 5-10 fold sequence redundancy assuming 250-300 base average read-lengths.

These purified DNA samples were then sequenced using the multiplex DNA sequencing based on chemical degradation methods (Church G.M. and Kieffer-Higgins S., Science 240:185-188, 1988) or by Sequithrem (Epicenter Technologies) dideoxy sequencing protocols. The sequencing reactions were electrophoresed and transferred onto nylon membranes by direct transfer electrophoresis from 40 cm gels (Richterich P. and Church G.M., Methods in Enzymology 218:187-222, 1993) or by electroblotting (Church, supra). 24 samples were run per gel. 45 successful membranes were produced by chemical sequencing and 8 were produced by dideoxy sequencing. The DNA was covalently bound to the membranes by exposure to ultraviolet light, and hybridized with labeled oligonucleotides complimentary to tag sequences on the vectors (Church, supra). The membranes were washed to rinse off non-specifically bound probe, and exposed to X-ray film to visualize individual sequence ladders. After autoradiography, the hybridized probe was removed by incubation at 65° C, and the hybridization cycle

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repeated with another tag sequence until the membrane had been probed 38 times for chemical sequencing membranes and 10 times for the dideoxy sequencing membranes. Thus, each gel produced a large number of films, each containing new sequencing information. Whenever a new blot was processed, it was initially probed for an internal standard sequence added to each of the pools.

Digital images of the films were generated using a laser-scanning densitometer (Molecular Dynamics, Sunnyvale, CA). The digitized images were processed on computer workstations (VaxStation 4000's) using the program REPLICA™ (Church et al., Automated DNA Sequencing and Analysis (J.C. Venter, ed.), Academic Press, 1994). Image processing included lane straightening, contrast adjustment to smooth out intensity differences, and resolution enhancement by iterative gaussian deconvolution. The sequences were then automatically picked in REPLICATM and displayed for interactive proofreading before being stored in a project database. The proofreading was accomplished by a quick visual scan of the film image followed by mouse clicks on the bands of the displayed image to modify the base calls. Many of the sequence errors could be detected and corrected because multiple sequence reads covering the same portion of the genomic DNA provide adequate sequence redundancy for editing. Each sequence automatically received an identification number (corresponding to microtiter plate, probe information, and lane set number). This number serves as a permanent identifier of the sequence so it is always possible to identify the original of any particular sequence without recourse to a specialized database.

Routine assembly of *H. pylori* sequences was done using the program FALCON (Church, Church et al., *Automated DNA Sequenicng and Analysis* (J.C. Venter, ed.), Academic Press, 1994). This program has proven to be fast and reliable for most sequences. The assembled contigs were displayed using a modified version of GelAssemble, developed by the Genetics Computer Group (GCG) (Devereux et al., *Nucleic Acid Res.* 12:387-95, 1984) that interacts with REPLICATM. This provided for an integrated editor that allows multiple sequence gel images to be instantaneously called up from the REPLICATM database and displayed to allow rapid scanning of contigs and proofreading of gel traces where discrepancies occurred between different sequence reads in the assembly.

II. Identification, cloning and expression of recombinant H. pylori DNA sequences

To facilitate the cloning, expression and purification of membrane and secreted proteins from *H. pylori* a powerful gene expression system, the pET System (Novagen), for cloning and expression of recombinant proteins in *E. coli*, was selected. Also, a DNA sequence encoding a peptide tag, the His-Tag, was fused to the 3' end of DNA

sequences of interest in order to facilitate purification of the recombinant protein products. The 3' end was selected for fusion in order to avoid alteration of any 5' terminal signal sequence. The exception to the above was ppiB, a gene cloned for use as a control in the expression studies. In this study, the sequence for *H. pylori* ppiB contains a DNA sequence encoding a His-Tag fused to the 5' end of the full length gene, because the protein product of this gene does not contain a signal sequence and is expressed as a cytosolic protein.

PCR Amplification and cloning of DNA sequences containing ORF's for membrane and secreted proteins from the J99 Strain of Helicobacter pylori.

Sequences chosen (from the list of the DNA sequences of the invention) for cloning from the J99 strain of H. pylori were prepared for amplification cloning by polymerase chain reaction (PCR). Synthetic oligonucleotide primers (Table 3) specific for the 5' and 3' ends of open reading frames (ORFs) were designed and purchased (GibcoBRL Life Technologies, Gaithersburg, MD, USA). All forward primers (specific 15 for the 5' end of the sequence) were designed to include an Ncol cloning site at the extreme 5' terminus, except for HpSeq. 4821082 where Ndel was used. These primers were designed to permit initiation of protein translation at a methionine residue followed by a valine residue and the coding sequence for the remainder of the native H. pylori DNA sequence. An exception is H. pylori sequence 4821082 where the initiator 20 methionine is immediately followed by the remainder of the native H. pylori DNA sequence. All reverse primers (specific for the 3' end of any H. pylori ORF) included a EcoRI site at the extreme 5' terminus to permit cloning of each H. pylori sequence into the reading frame of the pET-28b. The pET-28b vector provides sequence encoding an additional 20 carboxy-terminal amino acids (only 19 amino acids in HpSeq. 26380318 25 and HpSeq.14640637) including six histidine residues (at the extreme C-terminus), which comprise the His-Tag. An exception to the above, as noted earlier, is the vector construction for the ppiB gene. A synthetic oligonucleotide primer specific for the 5' end of ppiB gene encoded a BamHI site at its extreme 5' terminus and the primer for the 3' end of the ppiB gene encoded a XhoI site at its extreme 5' terminus. 30

<u>TABLE 3</u>
<u>Oligonucleotide primers used for PCR amplification of *H. pylori* DNA sequences</u>

Outer membrane Proteins	Forward primer 5' to 3'	Reverse Primer 5' to 3'
Protein 16225006	5'-TATACCATGGTGGG CGCTAA-3' (SEQ ID NO:147)	5'- ATGAATTCGAGTAAG GATTTTTG-3' (SEQ ID NO:148)
Protein 26054702	5'- TTAACCATGGTGAAA AGCGATA-3' (SEQ ID NO:149)	5'- TAGAATTCGCATAAC GATCAATC-3' (SEQ ID NO:150)
Protein 7116626	5'- ATATCCATGGTGAGT TTGATGA-3' (SEQ ID NO:151)	5'- ATGAATTCAATTTT TATTTTGCCA-3' (SEQ ID NO:152)
Protein 29479681	5'- AATTCCATGGTGGGG GCTATG-3' (SEQ ID NO:153)	5'- ATGAATTCTCGATAG CCAAAATC-3' (SEQ ID NO:154)
Protein 14640637	5'- AATTCCATGGTGCAT AACTTCCATT-3' (SEQ ID NO:155)	5'- AAGAATTCTCTAGCA TCCAAATGGA-3' (SEQ ID NO:156)
Periplasmic/ Secreted Proteins		
Protein 30100332	5'-ATTTCCATGGTCATG TCTCATATT-3' (SEQ ID NO:157)	5'- ATGAATTCCATCTTT TATTCCAC-3' (SEQ ID NO:158)
Protein 4721061	5'-AACCATGGTGATTT TAAGCATTGAAAG-3' (SEQ ID NO:159)	5'- AAGAATTCCACTCA AAATTTTTTAACAG-3' (SEQ ID NO:160)
Other Surface Proteins		·
Protein 4821082	5'-GATCATCCATATGTT ATCTTCTAAT-3' (SEQ ID NO:161)	5'- TGAATTCAACCATTT TAACCCTG-3' (SEQ ID NO:162)

Protein 978477	5'-TATACCATGGTGAA ATTTTTTCTTTTA-3' (SEQ ID NO:163)	5'- AGAATTCAATTGCG TCTTGTAAAAG-3' (SEQ ID NO:164)
Inner Membrane		
Protein		
Protein 26380318	5'-TATACCATGGTGAT	5'-ATGAATTCCCACTT
	GGACAAACTC-3' (SEQ	GGGGCGATA-3' (SEQ
	ID NO:165)	ID NO:166)
Cytoplasmic Protein		
	<u> </u>	
ppi	5'-TTATGGATCCAAAC	5'-TATCTCGAGTTATA
·	CAATTAAAACT-3' (SEQ	GAGAAGGGC-3' (SEO
	ID NO:167)	ID NO:168)

Genomic DNA prepared from the J99 strain of *H. pylori* (ATCC #55679; deposited by Genome Therapeutics Corporation, 100 Beaver Street, Waltham, MA 02154) was used as the source of template DNA for PCR amplification reactions

(Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., eds., 1994). To amplify a DNA sequence containing an *H. pylori* ORF, genomic DNA (50 nanograms) was introduced into a reaction vial containing 2 mM MgCl₂, 1 micromolar synthetic oligonucleotide primers (forward and reverse primers) complementary to and flanking a defined *H. pylori* ORF, 0.2 mM of each deoxynucleotide triphosphate; dATP, dGTP, dCTP, dTTP and 2.5 units of heat stable DNA polymerase (Amplitaq, Roche Molecular Systems, Inc., Branchburg, NJ, USA) in a final volume of 100 microliters. The following thermal cycling conditions were used to obtain amplified DNA products for each ORF using a Perkin Elmer Cetus/ GeneAmp PCR System 9600 thermal cycler:

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Protein 26054702, Protein 7116626, Protein 29479681, Protein 30100332, and Protein 4821082;

Denaturation at 94°C for 2 min,
2 cycles at 94°C for 15 sec, 30°C for 15 sec and 72°C for 1.5 min
20 23 cycles at 94°C for 15 sec, 55°C for 15 sec and 72°C for 1.5 min
Reactions were concluded at 72°C for 6 minutes.

Protein 16225006;

Denaturation at 94°C for 2 min.

25 cycles at 95°C for 15 sec, 55°C for 15 sec and 72°C for 1.5 min Reaction was concluded at 72°C for 6 minutes.

Protein 4721061;

Denaturation at 94°C for 2 min, 2 cycles at 94°C for 15 sec, 36°C for 15 sec and 72°C for 1.5 min 23 cycles at 94°C for 15 sec, 60°C for 15 sec and 72°C for 1.5 min Reactions were concluded at 72°C for 6 minutes.

Protein 26380318;

Denaturation at 94°C for 2 min, 2 cycles at 94°C for 15 sec, 38°C for 15 sec and 72°C for 1.5 min 23 cycles at 94°C for 15 sec, 62°C for 15 sec and 72°C for 1.5 min Reactions were concluded at 72°C for 6 minutes.

Protein 14640637;

Denaturation at 94°C for 2 min, 2 cycles at 94°C for 15 sec, 33°C for 15 sec and 72°C for 1.5 min 30 cycles at 94°C for 15 sec, 55°C for 15 sec and 72°C for 1.5 min Reactions were concluded at 72°C for 6 minutes.

Conditions for amplification of H. pylori ppiB;

Denaturation at 94°C for 2 min, 2 cycles at 94°C for 15 sec, 32°C for 15 sec and 72°C for 1.5 min 25 cycles at 94°C for 15 sec, 56°C for 15 sec and 72°C for 1.5 min Reactions were concluded at 72°C for 6 minutes

Upon completion of thermal cycling reactions, each sample of amplified DNA was washed and purified using the Qiaquick Spin PCR purification kit (Qiagen, Gaithersburg, MD, USA). All amplified DNA samples were subjected to digestion with the restriction endonucleases, Ncol and EcoRI (New England BioLabs, Beverly, MA, USA), or in the case of HpSeq. 4821082 (SEQ ID NO: 1309), with Ndel and EcoRI (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., eds., 1994). DNA samples were then subjected to electrophoresis on 1.0 % NuSeive (FMC BioProducts, Rockland, ME USA) agarose gels. DNA was visualized by exposure to ethidium bromide and long wave uv irradiation. DNA contained in slices

isolated from the agarose gel was purified using the Bio 101 GeneClean Kit protocol (Bio 101 Vista, CA, USA).

Cloning of H. pylori DNA sequences into the pET-28b prokaryotic expression vector.

The pET-28b vector was prepared for cloning by digestion with Ncol and EcoRI, or in the case of *H. pylori* protein 4821082 with Ndel and EcoRI (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., eds., 1994). In the case of cloning ppiB, the pET-28a vector, which encodes a His-Tag that can be fused to the 5' end of an inserted gene, was used and the cloning site prepared for cloning with the ppiB gene by digestion with BamHI and XhoI restriction endonucleases.

Following digestion, DNA inserts were cloned (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., eds., 1994) into the previously digested pET-28b expression vector, except for the amplified insert for ppiB, which was cloned into the pET-28a expression vector. Products of the ligation reaction were then used to transform the BL21 strain of *E. coli* (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., eds., 1994) as described below.

Transformation of competent bacteria with recombinant plasmids

Competent bacteria, *E coli* strain BL21 or *E. coli* strain BL21(DE3), were transformed with recombinant pET expression plasmids carrying the cloned *H. pylori* sequences according to standard methods (Current Protocols in Molecular, John Wiley and Sons, Inc., F. Ausubel et al., eds., 1994). Briefly, 1 microliter of ligation reaction was mixed with 50 microliters of electrocompetent cells and subjected to a high voltage pulse, after which, samples were incubated in 0.45 milliliters SOC medium (0.5% yeast extract, 2.0 % tryptone, 10 mM NaCl, 2.5 mM KCl, 10 mM MgCl2, 10 mM MgSO4 and 20, mM glucose) at 37°C with shaking for 1 hour. Samples were then spread on LB agar plates containing 25 microgram/ml kanamycin sulfate for growth overnight. Transformed colonies of BL21 were then picked and analyzed to evaluate cloned inserts as described below.

Identification of recombinant pET expression plasmids carrying H. pylori sequences

Individual BL21 clones transformed with recombinant pET-28b-H.pylori ORFs were analyzed by PCR amplification of the cloned inserts using the same forward and reverse primers, specific for each *H. pylori* sequence, that were used in the original PCR amplification cloning reactions. Successful amplification verified the integration of the *H. pylori* sequences in the expression vector (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., eds., 1994).

Isolation and Preparation of plasmid DNA from BL21 transformants

Individual clones of recombinant pET-28b vectors carrying properly cloned *H. pylori* ORFs were picked and incubated in 5 mls of LB broth plus 25 microgram/ml kanamycin sulfate overnight. The following day plasmid DNA was isolated and purified using the Qiagen plasmid purification protocol (Qiagen Inc., Chatsworth, CA, USA).

Expression of recombinant H. pylori sequences in E. coli

The pET vector can be propagated in any *E. coli* K-12 strain e.g. HMS174, HB101, JM109, DH5, etc. for the purpose of cloning or plasmid preparation. Hosts for expression include *E. coli* strains containing a chromosomal copy of the gene for T7 RNA polymerase. These hosts are lysogens of bacteriophage DE3, a lambda derivative that carries the lacI gene, the lacUV5 promoter and the gene for T7 RNA polymerase. T7 RNA polymerase is induced by addition of isopropyl-B-D-thiogalactoside (IPTG), and the T7 RNA polymerase transcribes any target plasmid, such as pET-28b, carrying a T7 promoter and a gene of interest. Strains used include: BL21(DE3) (Studier, F.W., Rosenberg, A.H., Dunn, J.J., and Dubendorff, J.W. (1990) Meth. Enzymol. 185, 60-89).

To express recombinant *H. pylori* sequences, 50 nanograms of plasmid DNA isolated as described above was used to transform competent BL21(DE3) bacteria as described above (provided by Novagen as part of the pET expression system kit). The lacZ gene (beta-galactosidase) was expressed in the pET-System as described for the *H. pylori* recombinant constructions. Transformed cells were cultured in SOC medium for 1 hour, and the culture was then plated on LB plates containing 25 micrograms/ml kanamycin sulfate. The following day, bacterial colonies were pooled and grown in LB medium containing kanamycin sulfate (25 micrograms/ml) to an optical density at 600 nM of 0.5 to 1.0 O.D. units, at which point, 1 millimolar IPTG was added to the culture for 3 hours to induce gene expression of the *H. pylori* recombinant DNA constructions.

After induction of gene expression with IPTG, bacteria were pelleted by centrifugation in a Sorvall RC-3B centrifuge at 3500 x g for 15 minutes at 4°C. Pellets were resuspended in 50 milliliters of cold 10 mM Tris-HCl, pH 8.0, 0.1 M NaCl and 0.1 mM EDTA (STE buffer). Cells were then centrifuged at 2000 x g for 20 min at 4°C. Wet pellets were weighed and frozen at -80°C until ready for protein purification.

III. Purification of recombinant proteins from E. coli Analytical Methods

The concentrations of purified protein preparations were quantified spectrophotometrically using absorbance coefficients calculated from amino acid

content (Perkins, S.J. 1986 Eur. J. Biochem. 157, 169-180). Protein concentrations were also measured by the method of Bradford, M.M. (1976) Anal. Biochem. 72, 248-254, and Lowry, O.H., Rosebrough, N., Farr, A.L. & Randall, R.J. (1951) J. Biol. Chem. 193, pages 265-275, using bovine serum albumin as a standard.

SDS-polyacrylamide gels (12% or 4.0 to 25 % acrylamide gradient gels) were purchased from BioRad (Hercules, CA, USA), and stained with Coomassie blue. Molecular weight markers included rabbit skeletal muscle myosin (200 kDa), *E. coli* (galactosidase (116 kDa), rabbit muscle phosphorylase B (97.4 kDa), bovine serum albumin (66.2 kDa), ovalbumin (45 kDa), bovine carbonic anhydrase (31 kDa), soybean trypsin inhibitor (21.5 kDa), egg white lysozyme (14.4 kDa) and bovine aprotinin (6.5 kDa).

1. Purification of soluble proteins

All steps were carried out at 4° C. Frozen cells were thawed, resuspended in 5 volumes of lysis buffer (20 mM Tris, pH 7.9, 0.5 M NaCl, 5 mM imidazole with 10% glycerol, 0.1 % 2-mercaptoethanol, 200 µg/ ml lysozyme, 1 mM phenylmethylsulfonyl fluoride (PMSF), and 10 µg/ml each of leupeptin, aprotinin, pepstatin, L-1-chloro-3-[4-tosylamido]-7-amino-2-heptanone (TLCK), L-1-chloro-3-[4-tosylamido]-4-phenyl-2-butanone (TPCK), and soybean trypsin inhibitor, and ruptured by several passages through a small volume microfluidizer (Model M-110S, Microfluidics International Corporation, Newton, MA). The resultant homogenate was made 0.1 % Brij 35, and centrifuged at 100,000 x g for 1 hour to yield a clear supernatant (crude extract).

Following filtration through a 0.8 µm Supor filter (Gelman Sciences, FRG) the crude extract was loaded directly onto a Ni²⁺⁻ nitrilotriacetate-agarose (NTA) with a 5 milliliter bed volume (Hochuli, E., Dbeli, H., and Schacheer, A. (1987) J. Chromatography 411, 177-184) pre-equilibrated in lysis buffer containing 10 % glycerol, 0.1 % Brij 35 and 1 mM PMSF. The column was washed with 250 ml (50 bed volumes) of lysis buffer containing 10 % glycerol, 0.1 % Brij 35, and was eluted with sequential steps of lysis buffer containing 10 % glycerol, 0.05 % Brij 35, 1 mM PMSF, and 20, 100, 200, and 500 mM imidazole in succession. Fractions were monitored by absorbance at OD₂₈₀ nm, and peak fractions were analyzed by SDS-PAGE. Fractions containing the recombinant protein eluted at 100 mM imidazole.

Recombinant protein 14640637 and proteins, beta-galactosidase (lacZ) and peptidyl-prolyl cis-trans isomerase (ppiB)

Fractions containing the recombinant proteins from the Ni²⁺-NTA-agarose columns were pooled and then concentrated to approximately 5 ml by centrifugal

filtration (Centriprep-10, Amicon, MA), and loaded directly onto a 180-ml column (1.6 X 91 cm) of Sephacryl S-100 HR gel filtration medium equilibrated in Buffer A (10 mM Hepes, pH 7.5, 150 mM NaCl, 0.1 mM EGTA) and run in Buffer A at 18 ml/h. Fractions containing the recombinant protein were identified by absorbance at 280 nm and analyzed by SDS-PAGE. Fractions were pooled and concentrated by centrifugal filtration.

Recombinant protein 7116626

Fractions containing the recombinant protein from the Ni²⁺-NTA-agarose column were pooled and dialyzed overnight against 1 liter of dialysis buffer (10 mM MOPS, pH 6.5, 50 mM NaCl, 0.1 mM EGTA, 0.02% Brij 35 and 1 mM PMSF). In the morning, a fine white precipitate was removed by centrifugation and the resulting supernatant was loaded onto an 8 ml (8 x 75 mm) MonoS high performance liquid chromatography column (Pharmacia Biotechnology, Inc., Piscataway, NJ, USA) equilibrated in buffer B (10 mM MOPS, pH 6.5, 0.1 mM EGTA) containing 50 mM NaCl. The column was washed with 10 bed volumes of buffer B containing 50 mM NaCl, and developed with a 50-ml linear gradient of increasing NaCl (50 to 500 mM). Recombinant protein 7116626 eluted as a sharp peak at 300 mM NaCl.

2. Purification of insoluble proteins from inclusion bodies

The following steps were carried out at 4°C. Cell pellets were resuspended in lysis buffer with 10% glycerol 200 µg/ ml lysozyme, 5 mM EDTA, 1mM PMSF and 0.1% -mercaptoethanol. After passage through the cell disrupter, the resulting homogenate was made 0.2% deoxycholate, stirred 10 minutes, then centrifuged at 20,000 x g, for 30 min. The pellets were washed with lysis buffer containing 10% glycerol, 10 mM EDTA, 1% Triton X-100, 1 mM PMSF and 0.1% -mercaptoethanol, followed by several washes with lysis buffer containing 1 M urea, 1 mM PMSF and 0.1% 2-mercaptoethanol. The resulting white pellet was composed primarily of inclusion bodies, free of unbroken cells and membranous materials..

Recombinant proteins 26054702, 16225006, 30100332, 4721061

The following steps were carried out at room temperature. Purified inclusion bodies were dissolved in 20 ml 8.0 M urea in lysis buffer with 1 mM PMSF and 0.1 % 2-mercaptoethanol, and incubated at room temperature for 1 hour. Materials that did not dissolve were removed by centrifugation. The clear supernatant was filtered, then loaded onto a Ni²⁺-NTA agarose column pre-equilibrated in 8.0 M urea in Lysis Buffer. The column was washed with 250 ml (50 bed volumes) of lysis buffer

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containing 8 M urea, 1.0 mM PMSF and 0.1 % 2-mercaptoethanol, and developed with sequential steps of lysis buffer containing 8M urea, 1 mM PMSF, 0.1 % 2-mercaptoethanol and 20, 100, 200, and 500 mM imidazole in succession. Fractions were monitored by absorbance at OD₂₈₀ nm, and peak fractions were analyzed by SDS-PAGE. Fractions containing the recombinant protein eluted at 100 mM imidazole.

Recombinant proteins 29479681, 26380318

The pellet containing the inclusion bodies was solubilized in buffer B containing 8 M urea, 1 mM PMSF and 0.1 % 2-mercaptoethanol, and incubated for 1 hour at room temperature. Insoluble materials were removed by centrifugation at 20,000 x g for 30 min, and the cleared supernatant was loaded onto a 15 ml (1.6 x 7.5 cm) SP-Sepharose column pre-equilibrated in buffer B, 6 M urea, 1 mM PMSF, 0.1 % 2-mercaptoethanol. After washing the column with 10 bed volumes, the column was developed with a linear gradient from 0 to 500 mM NaCl.

15 Dialysis and concentration of protein samples

Urea was removed slowly from the protein samples by dialysis against Trisbuffered saline (TBS; 10 mM Tris pH 8.0, 150 mM NaCl) containing 0.5 % deoxycholate (DOC) with sequential reduction in urea concentration as follows; 6M, 4M, 3M, 2M, 1M, 0.5 M and finally TBS without any urea. Each dialysis step was conducted for a minimum of 4 hours at room temperature.

After dialysis, samples were concentrated by pressure filtration using Amicon stirred-cells. Protein concentrations were measured using the methods of Perkins (1986 Eur. J. Biochem. 157, 169-180), Bradford ((1976) Anal. Biochem. 72, 248-254) and Lowry ((1951) J. Biol. Chem. 193, pages 265-275).

The recombinant proteins purified by the methods described above are summarized in Table 4 below.

TABLE 4

J99 Sequence Identifier Outer Memb	Homolog identified by Blast brane Protein	Gene symbol of Homolog	Bacterial cell fraction used to purify recombinant proteins	Method of purification	Relative MW on SDS- PAGE gel	Final concentratio n of purified protein	Composit ionof buffer
16225006	P28635	YEAC	Inclusion bodies	His-Tag	18 kDa	5 mg/ml	В
26054702	P15929	flgH	Inclusion bodies	His-Tag	37 kDa	1.18 mg/ml	В

<u></u>	т		T				
	ļ			}			as dry
		 		 	· · · · · ·	<u> </u>	pellet
7116626	P26093	e(P4)	Soluble fraction	His-Tag	29 kDa	0.8/1	<u> </u>
7110020	120073	(14)	Soldole Haction	mis-tag	29 KDa	0.8 mg/ml	A C
		 				1.85 mg/ml	<u> </u>
29479681	P13036	fecA	Inclusions	SP-	23 kDa	2 26 2/1	В
2,47,001	113030	, acta	bodies	Sepharose	23 KDa	2.36 mg/ml	D
		 	Doules	Sepharose		0.5	В
		 				0.5 mg ml	
		•		į			as dry pellet
		 		·			pener
14640637	P16665	TPF1	Soluble fraction	His-Tag	17 kDa	2.4 mg/ml	A
14040037	110005		Soldole Haction		ion S100 HR	2.4 mg/ml	Α
		<u> </u>		germinan	I SIOU DK	 	
Perinlasmic/	Secreted Pro	tein	1		<u>L</u>	l	
· ci ipiasmici	Secreteu F FO	icin	1		T		
3010032	P23847	denA	Inclusion hadis-	Hio To-	11150	2.00 / 1	- 6
3010032	F430 4 1	dppA	Inclusion bodies	His-Tag	ll kDa	2.88 mg/ml	B
4721061	P36175	GCP	Inchesion budies	11: 7	2015		
4/21001	F30173	GCF	Inclusion bodies	His-Tag	38 kDa	2.8 mg/ml	В
Other Surfac	Duotoina	<u> </u>			<u></u>	<u> </u>	
Other Suriat	e Froteins	 				<u> </u>	
4821082	P08089	M	31111	11: 7	2015		
4021002	PU8089	1	Inclusion bodies	His-Tag	20 kDa	1.16 mg/ml	В
		protein					
978477	L28919	FBP54	Inclusion hadias	CD	441.75-	2.56 ()	
710411	L20919	FBF54	Inclusion bodies	SP-	44 kDa	2.56 mg/ml	В
		 		Sepharose		. 0.2/1	B
Inner Memb	rane Protein:	<u></u>	<u> </u>			0.3 mg/ml	<u> </u>
Inner West	inne i totein	, 				· · · · · · · · · · · · · · · · · · ·	-
26380318	P15933	NiG	Inclusion bodies	SP-	11 kDa	22 2/ 1	р
20300316	1 13933	l mo	inclusion bodies	Sepharose	11 KDa	22 mg/ml	В
		 		Sepharose			
					· · · · · · · · · · · · · · · · · · ·		
Control Prot	eins with His	Teg	<u> </u>				
	Cins With Tils	I.					
	P00722	lacZ	Soluble fraction	His-Tag	116 kDa	10 mg/ml	A
	100/22		Soluble Haction		on S200 HR	to mg/mi	- А
<u>-</u>		 		ger muan	UII 3200 MK	1	
		ppiB	Soluble fraction	His-Tag	21 kDa	4.4 mg/ml	Α
		Phin	COMO HACHON		on S100 HR	7.7 mg/m	
Buffer	·			ger muan	און ממוכיוים		
composition							
S:						.]	
	nes nH 7 5 1	50 mM Na	Cl, 0.1 mM EGTA	₁			
			1, 0.5 % DOC			+	
			aCl, 0.1 EGTA		 		•
C 10 111141 141	J. J. Pi I U.J., .	AND INIAI IA	ICI, V.I ECIA		 -		
		L					

IV. Analysis of H. pylori proteins as Vaccine candidates

To investigate the immunomodulatory effect of *H. pylori* proteins, a mouse/*H. pylori* model was used. This model mimics the human *H. pylori* infection in many respects. The focus is on the effect of oral immunization in *H. pylori* infected animals in order to test the concept of therapeutic oral immunotherapy.

Animals

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Female SPF BALB/c mice were purchased from Bomholt Breeding center (Denmark). They were kept in ordinary makrolon cages with free supply of water and food. The animals were 4-6 weeks old at arrival.

Infection

After a minimum of one week of acclimatization, the animals were infected with a type 2 strain (VacA negative) of *H. pylori* (strain 244, originally isolated from an ulcer patient). In our hands, this strain has earlier proven to be a good colonizer of the mouse stomach. The bacteria were grown overnight in Brucella broth supplemented with 10 % fetal calf serum, at 37°C in a microaerophilic atmosphere (10% CO₂, 5%O₂). The animals were given an oral dose of omeprazole (400 µmol/kg) and 3-5 h after this an oral inoculation of *H. pylori* in broth (approximately 10⁸ cfu/animal). Positive take of the infection was checked in some animals 2-3 weeks after the inoculation.

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Antigens

Recombinant *H. pylori* antigens were chosen based on their association with externally exposed *H. pylori* cell membrane. These antigens were selected from the following groups: (1.) Outer Membrane Proteins; (2.) Periplastic/Secreted proteins; (3.) Outer Surface proteins; and (4.) Inner Membrane proteins. All recombinant proteins were constructed with a hexa-HIS tag for purification reasons and the non-*Helicobacter pylori* control protein (b-galactosidase from *E. coli*; LacZ), was constructed in the same way.

All antigens were given in a soluble form, i.e. dissolved in either a HEPES buffer or in a buffer containing 0.5% Deoxycholate (DOC).

The antigens are listed in Table 5 below.

<u>Table 5</u>
<u>Helicobacter pylori proteins</u>

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Outer membrane Proteins Protein 7116626 Protein 4721061 Protein 16225006 Protein 29479681 Protein 14640637

5 Periplasmic/Secreted Proteins

Protein 30100332

Other cell envelope proteins

Protein 4821082

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Flagella-associated proteins

Protein 26380318

Control proteins

15 b-galactosidase (LacZ)

Immunizations

Ten animals in each group were immunized 4 times over a 34 day period (day 1, 15, 25 and 35). Purified antigens in solution or suspension were given at a dose of 100 mg/mouse. As an adjuvant, the animals were also given 10 µg/mouse of Cholera toxin (CT) with each immunization. Omeprazole (400 mmol/kg) was given orally to the animals 3-5 h prior to immunization as a way of protecting the antigens from acid degradation. Infected control animals received HEPES buffer + CT or DOC buffer + CT. Animals were sacrificed 2-4 weeks after final immunization. A general outline of the study is shown in Table 6 below.

<u>Table 6</u>
<u>Study outline, therapeutic immunization:</u>

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Mice were all infected with H. pylori strain Ah244 at day 30.

- 2 E	Substance	Mouse strain n=10	Dose/mouse	Dates for dosing
35	1. Controls, PBS	Balb/c	0.3 ml	0, 14, 24, 34
	2. Cholera toxin, 10 μg	Balb/c	0.3 ml	0, 14, 24, 34
40	3. Protein 16225006, 100 μg + CT 1	0 μg Balb/c	0.3 ml	0, 14, 24, 34
	4. Protein 26054702, 100 μg + CT 1	0 μg Balb/c	0.3 ml	0, 14, 24, 34

	5. Protein 26380318, 100 μg + CT 10 μg Balb/c	0.3 ml	0, 14, 24, 34
٠	6. Protein 29479681, 100 μg + CT 10 μg Balb/c	0.3 ml	0, 14, 24, 34
5	7. Protein 30100332, 100 μg + CT 10 μg Balb/c	0.3 ml	0, 14, 24, 34
•	8. Protein 4721061, 100 μg + CT 10 μg Balb/c	0.3 ml	0, 14, 24, 34
10	9. Protein 4821082, 100 μg + CT 10 μg Balb/c	0.3 ml	0, 14, 24, 34
10	10. Protein 7116626, 100 μg + CT 10 μg Balb/c	0.3 ml	0, 14, 24, 34
	11.Protein 14640637, 100 μg + CT 10 μg Balb/c	0.3 ml	0, 14, 24, 34

15 Analysis of infection

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Mucosal infection: The mice were sacrificed by CO₂ and cervical dislocation. The abdomen was opened and the stomach removed. After cutting the stomach along the greater curvature, it was rinsed in saline. The mucosa from the antrum and corpus of an area of 25mm² was scraped separately with a surgical scalpel. The mucosa scraping was suspended in Brucella broth and plated onto Blood Skirrow selective plates. The plates were incubated under microaerophilic conditions for 3-5 days and the number of colonies was counted. The identity of *H. pylori* was ascertained by urease and catalase test and by direct microscopy or Gram staining.

The urease test was performed essentially as follows. The reagent, Urea Agar Base Concentrate, was purchased from DIFCO Laboratories, Detroit, MI (Catalog # 0284-61-3). Urea agar base concentrate was diluted 1:10 with water. 1 ml of if the diluted concentrate was mixed with 100-200 ml of actively growing *H. pylori* cells. Color change to magenta indicated that cells were urease positive.

The catalase test was performed essentially as follows. The reagent, N,N,N',N'-Tetramethyl-p-Phenylenediamine, was purchased from Sigma, St. Louis, MO (Catalog # T3134). A solution of the regent (1% w/v in water) was prepared. *H. pylori* cells were swabbed onto Whatman filter paper and overlaid with the 1% solution. Color change to dark blue indicated that the cells were catalase positive.

<u>Serum antibodies:</u> From all mice serum was prepared from blood drawn by heart puncture. Serum antibodies were identified by regular ELISA techniques, where the specific antigens of *Helicobacter pylori* were plated.

Mucosal antibodies: Gentle scrapings of a defined part of the corpus and of 4 cm of duodenum were performed in 50% of the mice in order to detect the presence of

antibodies in the mucous. The antibody titers were determined by regular ELISA technique as for serum antibodies.

Statistical analysis: Wilcoxon-Mann-Whitney sign rank test was used for determination of significant effects of the antigens on *Helicobacter pylori* colonization. P<0.05 was considered significant. Because the antrum is the major colonization site for *Helicobacter* most emphasis was put upon changes in the antral colonization.

Results

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Antibodies in sera: All antigens tested given together with CT gave rise to a measurable specific titer in serum. The highest responses were seen with Protein 7116626, Protein 4721061, Protein 26380318, Protein 14640637 and Protein 4821082 (see Figure 1).

Antibodies in mucus: In the mucus scrapings, specific antibodies against all antigens tested were seen. By far the strongest response was seen with Protein 30100332, followed by Protein 14640637, and Protein 26380318 (see Figure 2).

Therapeutic immunization effects:

All control animals (BALB/c mice) were well colonized with *H. pylori* (strain AH244) in both antrum and corpus of the stomach. Of the antigens tested 3 proteins (Protein 4721061, Protein 4821082, and Protein 14640637) gave a good and significant reduction and/or eradication of the *H. pylori* infection. The degree of colonization of the antrum was lower following immunization with Protein 7116626 and Protein 26380318 compared to control. The effect of Proteins 16225006, 29479681, and 30100332 did not differ from control. The control protein lacZ, i.e. the non-*H. pylori* protein, had no eradication effect and in fact had higher *Helicobacter* colonization compared to the HEPES + CT control. All data are shown in Figures 3 and 4 for proteins dissolved in HEPES and DOC respectively. Data is shown as geometric mean values. n=8-10 Wilcoxon-Mann-Whitney sign rank test * = p<0.05; x/10 = number of mice showing eradication of *H. pylori* over the total number of mice examined.

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The data presented indicate that all of the *H. pylori* associated proteins included in this study, when used as oral immunogens in conjunction with the oral adjuvant CT, resulted in stimulation of an immune response as measured by specific serum and mucosal antibodies. A majority of the proteins led to a reduction, and in some cases complete clearance of the colonization of *H. pylori* in this animal model. It should be noted that the reduction or clearance was due to heterologous protection rather than homologous protection (the polypeptides were based on the *H. pylori* J99 strain

sequence and used in the therapeutic immunization studies against a different (AH244) challenge strain, indicating the vaccine potential against a wide variety of *H. pylori* strains.

The highest colonization in the antrum was seen in animals treated with the non-Helicobacter protein LacZ, indicating that the effects seen with the Helicobacter pylori antigens were specific.

Taken together these data strongly support the use of these *H. pylori* proteins in a pharmaceutical formulation for the use in humans to treat and/or prevent *H. pylori* infections.

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V. Sequence Variance Analysis of genes in Helicobacter pylori strains

Four genes were cloned and sequenced from several strains of *H. pylori* to compare the DNA and deduced amino acid sequences. This information was used to determine the sequence variation between the *H. pylori* strain, J99, and other *H. pylori* strains isolated from human patients.

Preparation of Chromosomal DNA.

Cultures of *H. pylori* strains (as listed in Table 9) were grown in BLBB (1% Tryptone, 1% Peptamin 0.1% Glucose, 0.2% Yeast Extract 0.5% Sodium Chloride, 5% Fetal Bovine Serum) to an OD₆₀₀ of 0.2. Cells were centrifuged in a Sorvall RC-3B at 3500 x g at 4°C for 15 minutes and the pellet resuspended in 0.95 mls of 10 mM Tris-HCl, 0.1 mM EDTA (TE). Lysozyme was added to a final concentration of 1mg/ml along with, SDS to 1% and RNAse A + T1 to 0.5mg/ml and 5 units/ml respectively, and incubated at 37°C for one hour. Proteinase K was then added to a final concentration of 0.4mg/ml and the sample was incubated at 55 C for more than one hour. NaCl was added to the sample to a concentration of 0.65 M, mixed carefully, and 0.15 ml of 10% CTAB in 0.7M NaCL (final is 1% CTAB/70mM NaCL) was added followed by incubation at 65°C for 20 minutes. At this point, the samples were extracted with chloroform:isoamyl alcohol, extracted with phenol, and extracted again with chloroform:isoamyl alcohol. DNA was precipitated with either EtOH (1.5 x volumes) or isopropanol (0.6 x volumes) at -70°C for 10minutes, washed in 70% EtOH and resuspended in TE.

PCR Amplification and cloning.

Genomic DNA prepared from twelve strains of *Helicobacter pylori* was used as the source of template DNA for PCR amplification reactions (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994). To

amplify a DNA sequence containing an *H. pylori* ORF, genomic DNA (10 nanograms) was introduced into a reaction vial containing 2 mM MgCl₂, 1 micromolar synthetic oligonucleotide primers (forward and reverse primers, see Table 7) complementary to and flanking a defined *H. pylori* ORF, 0.2 mM of each deoxynucleotide triphosphate; dATP, dGTP, dTTP and 0.5 units of heat stable DNA polymerase (Amplitaq, Roche Molecular Systems, Inc., Branchburg, NJ, USA) in a final volume of 20 microliters in duplicate reactions.

Table 7

Oligonucleotide primers used for PCR amplification of *H. pylori* DNA sequences.

Outer membrane	Forward primer 5' to 3'	Reverse Primer 5' to 3'
Proteins		
	· .	
Protein 26054702 (for	5'-	5'-
strains AH4, AH15,	TTAACCATGGTGAAA	TAGAATTCGCCTCTA
AH61, 5294, 5640,	AGCGATA-3' (SEQ ID	AAACTTTAG-3' (SEQ
AH18, and AH244)	NO:169)	ID NO:170)
D	51	
Protein 26054702	5'-	5'-
(for strains AH5, 5155,	TTAACCATGGTGAAA	TAGAATTCGCATAAC
7958, AH24, and J99)	AGCGATA-3' (SEQ ID	GATCAATC-3' (SEQ ID
	NO:171)	NO:172)
D	l <u>"</u> .	
Protein 7116626	5'-	5'-
	ATATCCATGGTGAGT	ATGAATTCAATTTTT
	TTGATGA-3' (SEQ ID	TATTTTGCCA-3' (SEQ
	NO:173)	ID NO:174)
Protein 29479681	5'-	5'-
1 10tcm 25475001	AATTCCATGGCTATC	ATGAATTCGCCAAAA
	CAAATCCG-3' (SEQ ID	TCGTAGTATT-3' (SEQ
	NO:175)	• • • • • • • • • • • • • • • • • • • •
	110.173)	ID NO:176)
Protein 346	5'-	5'-
	GATACCATGGAATTT	TGAATTCGAAAAAGT
·	ATGAAAAAG-3' (SEQ	GTAGTTATAC-3' (SEQ
	ID NO:177)	ID NO:178)

The following thermal cycling conditions were used to obtain amplified DNA products for each ORF using a Perkin Elmer Cetus/ GeneAmp PCR System 9600 thermal cycler:

Protein 7116626 and Protein 346;

Denaturation at 94°C for 2 min,

2 cycles at 94°C for 15 sec, 30°C for 15 sec and 72°C for 1.5 min

23 cycles at 94°C for 15 sec, 55°C for 15 sec and 72°C for 1.5 min

Reactions were concluded at 72°C for 6 minutes.

Protein 26054702 for strains AH5, 5155, 7958, AH24, and J99; Denaturation at 94°C for 2 min,

2 cycles at 94°C for 15 sec, 30°C for 15 sec and 72°C for 1.5 min 25 cycles at 94°C for 15 sec, 55°C for 15 sec and 72°C for 1.5 min Reaction was concluded at 72°C for 6 minutes.

Protein 26054702 and Protein 294796813 for strains AH4, AH15, AH61, 5294, 5640, AH18, and Hp244;

Denaturation at 94°C for 2 min, 2 cycles at 94°C for 15 sec, 30°C for 20 sec and 72°C for 2 min 25 cycles at 94°C for 15 sec, 55°C for 20 sec and 72°C for 2 min Reactions were concluded at 72°C for 8 minutes.

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Upon completion of thermal cycling reactions, each pair of samples were combined and used directly for cloning into the pCR cloning vector as described below.

Cloning of H. pylori DNA sequences into the pCR TA cloning vector.

All amplified inserts were cloned into the pCR 2.1 vector by the method described in the Original TA cloning kit (Invitrogen, San Diego, CA). Products of the ligation reaction were then used to transform the TOP10F' (INVaF' in the case of H. pylori sequence 350) strain of E. coli as described below.

30 Transformation of competent bacteria with recombinant plasmids

Competent bacteria, E coli strain TOP10F' or E. coli strain INVaF' were transformed with recombinant pCR expression plasmids carrying the cloned H. pylori sequences according to standard methods (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994). Briefly, 2 microliters of 0.5 micromolar BME was added to each vial of 50 microliters of competent cells. Subsequently, 2 microliters of ligation reaction was mixed with the competent cells and incubated on ice for 30 minutes. The cells and ligation mixture were then subjected to a

"heat shock" at 42°C for 30 seconds, and were subsequently placed on ice for an additional 2 minutes, after which, samples were incubated in 0.45 milliliters SOC medium (0.5% yeast extract, 2.0 % tryptone, 10 mM NaCl, 2.5 mM KCl, 10 mM MgCl2, 10 mM MgSO4 and 20, mM glucose) at 37°C with shaking for 1 hour. Samples were then spread on LB agar plates containing 25 microgram/ml kanamycin sulfate or 100 micrograms/ml ampicillan for growth overnight. Transformed colonies of TOP10F' or INVaF' were then picked and analyzed to evaluate cloned inserts as described below. *Identification of recombinant PCR plasmids carrying H. pylori sequences*

Individual TOP10F' or INVaF' clones transformed with recombinant pCR-H.pylori ORFs were analyzed by PCR amplification of the cloned inserts using the same forward and reverse primers, specific for each H. pylori sequence, that were used in the original PCR amplification cloning reactions. Successful amplification verified the integration of the H. pylori sequences in the cloning vector (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994).

Individual clones of recombinant pCR vectors carrying properly cloned *H. pylori* ORFs were picked for sequence analysis. Sequence analysis was performed on ABI Sequencers using standard protocols (Perkin Elmer) using vector-specific primers (as found in PCRII or pCR2.1, Invitrogen, San Diego, CA) and sequencing primers specific to the ORF as listed in Table 8 below.

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<u>Table 8</u>
<u>Oligonucleotide primers used for sequencing of H. pylori DNA sequences.</u>

Outer membrane	Forward primers 5' to 3'	Reverse Primers 5' to 3'
Proteins	volumera 2, fo 2,	Acverse reimers 5, to 3,
1 I OCCIUS		
Protein 26054702	5'-	5'-
	CCCTTCATTTTAGAAATC	CTTTGGGTAAAAACGCA
	G-3' (SEQ ID NO:179)	TC-3' (SEQ ID NO:186)
	5'-	5'-
	ATTTCAACCAATTCAAT	CGATCTTTGATCCTAATT
,	GCG-3' (SEQ ID NO:180)	CA-3' (SEQ ID NO:187)
	5'-	5'-
	GCCCCTTTTGATTTGAAG	ATCAAGTTGCCTATGCT
	CT-3' (SEQ ID NO:181)	GA-3' (SEQ ID NO:188)
•	5'-	
	TCGCTCCAAGATACCAA	
	GAAGT-3' (SEQ ID	
	NO:182)	
	5'-	
	CTTGAATTAGGGGCAAA	
	GATCG-3' (SEQ ID	
	NO:183)	
	5'-	
	ATGCGTTTTTACCCAAA	
	GAAGT-3' (SEQ ID	·
	NO:184)	
	5'-	
	ATAACGCCACTTCCTTAT	
•	TGGT-3' (SEQ ID NO:185)	
	10010 (000 10 100:100)	
Protein 7116626	5'-	5'-
· · · · · · · · · · · · · · · · · · ·	TTGAACACTTTTGATTAT	"
		GTCTTTAGCAAAAATGG
•	GCGG-3' (SEQ ID NO:189) 5'+	CGTC-3' (SEQ ID NO:191)
		5'-
•	GGATTATGCGATTGTTTT	AATGAGCGTAAGAGAGC
-	ACAAG-3' (SEQ ID	CTTC-3' (SEQ ID NO:192)
Duradada	NO:190)	
Protein	5'-	5'-
29479681	CTTATGGGGGTATTGTC	AGGTTGTTGCCTAAAGA
	A-3' (SEQ ID NO:193)	CT-3' (SEQ ID NO:195)
	5'-	5'-
	AGCATGTGGGTATCCAG	CTGCCTCCACCTTTGATC
	C-3' (SEQ ID NO:194)	-3' (SEQ ID NO:196)

Protein 346	5'- ACCAATATCAATTGGCA CT-3' (SEQ ID NO:197) 5'- ACTTGGAAAAGCTCTGC A-3' (SEQ ID NO:198)	5'- CTTGCTTGTCATATCTAG C-3' (SEQ ID NO:199) 5'- GTTGAAGTGTTGGTGCT A-3' (SEQ ID NO:200)
	5'- CAAGCAAGTGGTTTGGT TTTAG-3' (SEQ ID NO:201) 5'- TGGAAAGAGCAAATCAT TGAAG-3' (SEQ ID NO:202)	5'- GCCCATAATCAAAAAGC CCAT-3' (SEQ ID NO:203) 5'- CTAAAAACCAAACCACTT GCT TGTC-3' (SEQ ID NO:204)
Vector Primers	5'- GTAAAACGACGGCCAG- 3' (SEQ ID NO:205)	5'- CAGGAAACAGCTATGAC -3' (SEQ ID NO:206)

Results

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To establish the PCR error rate in these experiments, five individual clones of Protein 26054702, prepared from five separate PCR reaction mixtures from *H. pylori* strain J99, were sequenced over a total length of 897 nucleotides for a cumulative total of 4485 bases of DNA sequence. DNA sequence for the five clones was compared to a DNA sequence obtained previously by a different method, i.e., random shotgun cloning and sequencing. The PCR error rate for the experiments described herein was determined to be 2 base changes out of 4485 bases, which is equivalent to an estimated error rate of less than or equal to 0.04%.

DNA sequence analysis was performed on four different open reading frames identified as genes and amplified by PCR methods from a dozen different strains of the bacterium *Helicobacter pylori*. The deduced amino acid sequences of three of the four open reading frames that were selected for this study showed statistically significant BLAST homology to defined proteins present in other bacterial species. Those ORFs included: Protein 26054702, homologous to the val A & B genes encoding an ABC transporter in F. novicida; Protein 7116626, homologous to lipoprotein e (P4) present in the outer membrane of H. influenzae; Protein 29479681, homologous to fecA, an outer membrane receptor in iron (III) dicitrate transport in *E. coli*. Protein 346 was identified as an unknown open reading frame, because it showed low homology with sequences in the public databases.

To assess the extent of conservation or variance in the ORFs across various strains of *H. pylori*, changes in DNA sequence and the deduced protein sequence were compared to the DNA and deduced protein sequences found in the J99 strain of *H*.

pylori (see Table 9 below). Results are presented as percent identity to the J99 strain of H. pylori sequenced by random shotgun cloning. To control for any variations in the J99 sequence each of the four open reading frames were cloned and sequenced again from the J99 bacterial strain and that sequence information was compared to the sequence information that had been collected from inserts cloned by random shotgun sequencing of the J99 strain. The data demonstrate that there is variation in the DNA sequence ranging from as little as 0.12 % difference (Protein 346, J99 strain) to approximately 7% change (Protein 26054702, strain AH5). The deduced protein sequences show either no variation (Protein 346, strains AH18 and AH24) or up to as much as 7.66% amino acid changes (Protein 26054702, Strain AH5).

Table 9

J99 Protein #	26054702	2054702	7116626	7116626 2	29479681	29479681	346 3	46
Length of Re Sequenced:	_	746 nt.	232 a.a.	96 nt.	182 a.a.	548 nt. 2	273 a.a. 81	9 nt.
Strain Tested	AA identity	Nuc.	AA identity	Nuc.	AA identity	Nuc.	AA identity	Nuc.
J99	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	99.63%	99.88%
AH244	95.16%	95.04%	n.d.	n.d.	99.09%	96.71%	98.90%	96.45%
AH4	95.97%	95.98%	97.84%	95.83%	n.d.	n.d.	97.80%	95.73%
AH5	92.34%	93.03%	98.28%	96.12%	98.91%	96.90%	98.53%	95.73%
AH15	95.16%	94.91%	97.41%	95.98%	99.82%	97.99%	99.63%	96.09%
AH61	n.d.	n.d.	97.84%	95.98%	99.27%	97.44%	n.d.	n.d.
5155	n.d.	n.d.	n.d.	n.d.	99.45%	97.08%	98.53%	95.60%
5294	94.35%	94.37%	98.28%	95.40%	99.64%	97.26%	97.07%	95.48%
7958	94.35%	94.10%	97.84%	95.40%	n.d.	n.d.	99.63%	96.46%
5640	95.16%	94.37%	97.41%	95.69%	99.09%	97.63%	98.53%	95.48%
AH18	n.d.	n.d.	98.71%	95.69%	99.64%	97.44%	100.00%	95.97%
AH24	94.75%	95.04%	97.84%	95.40%	99.27%	96.71%	100.00%	96.46%

n.d.= not done.

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VI. Experimental Knock-Out Protocol for the Determination of Essential H. pylori Genes as Potential Therapeutic Targets

Therapeutic targets are chosen from genes whose protein products appear to play key roles in essential cell pathways such as cell envelope synthesis, DNA synthesis, transcription, translation, regulation and colonization/virulence.

The protocol for the deletion of portions of *H. pylori* genes/ORFs and the insertional mutagenesis of a kanamycin-resistance cassette in order to identify genes which are essential to the cell is modified from previously published methods (Labigne-Roussel et al., 1988, J. Bacteriology 170, pp. 1704-1708; Cover et al., 1994, J. Biological Chemistry 269, pp. 10566-10573; Reyrat et al., 1995, Proc. Natl. Acad. Sci. 92, pp 8768-8772). The result is a gene "knock-out."

Identification and Cloning of H. pylori Gene Sequences

The sequences of the genes or ORFs (open reading frames) selected as knock-out targets are identified from the *H. pylori* genomic sequence and used to design primers to specifically amplify the genes/ORFs. All synthetic oligonucleotide primers are designed with the aid of the OLIGO program (National Biosciences, Inc., Plymouth, MN 55447, USA), and can be purchased from Gibco/BRL Life Technologies (Gaithersburg, MD, USA). If the ORF is smaller than 800 to 1000 base pairs, flanking primers are chosen outside of the open reading frame.

Genomic DNA prepared from the *Helicobacter pylori* HpJ99 strain (ATCC 55679; deposited by Genome Therapeutics Corporation, 100 Beaver Street, Waltham, MA 02154) is used as the source of template DNA for amplification of the ORFs by PCR (polymerase chain reaction) (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994). For the preparation of genomic DNA from *H. pylori*, see Example I. PCR amplification is carried out by introducing 10 nanograms of genomic HpJ99 DNA into a reaction vial containing 10 mM Tris pH 8.3, 50 mM KCl, 2 mM MgCl₂, 2 microMolar synthetic oligonucleotide primers (forward=F1 and reverse=R1), 0.2 mM of each deoxynucleotide triphosphate (dATP,dGTP, dCTP, dTTP), and 1.25 units of heat stable DNA polymerase (Amplitaq, Roche Molecular Systems, Inc., Branchburg, NJ, USA) in a final volume of 40 microliters. The PCR is carried out with Perkin Elmer Cetus/GeneAmp PCR System 9600 thermal cyclers.

Upon completion of thermal cycling reactions, each sample of amplified DNA is visualized on a 2% TAE agarose gel stained with Ethidium Bromide (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994) to

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determine that a single product of the expected size had resulted from the reaction. Amplified DNA is then washed and purified using the Qiaquick Spin PCR purification kit (Qiagen, Gaithersburg, MD, USA).

PCR products are cloned into the pT7Blue T-Vector (catalog#69820-1, Novagen, Inc., Madison, WI, USA) using the TA cloning strategy (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994). The ligation of the PCR product into the vector is accomplished by mixing a 6 fold molar excess of the PCR product, 10 ng of pT7Blue-T vector (Novagen), 1 microliter of T4 DNA Ligase Buffer (New England Biolabs, Beverly, MA, USA), and 200 units of T4 DNA Ligase (New England Biolabs) into a final reaction volume of 10 microliters. Ligation is allowed to proceed for 16 hours at 16°C.

Ligation products are electroporated (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994) into electroporation-competent XL-1 Blue or DH5-a *E.coli* cells (Clontech Lab., Inc. Palo Alto, CA, USA). Briefly, 1 microliter of ligation reaction is mixed with 40 microliters of electrocompetent cells and subjected to a high voltage pulse (25 microFarads, 2.5 kV, 200 ohms) after which the samples are incubated in 0.45 ml SOC medium (0.5% yeast extract, 2% tryptone, 10 mM NaCl, 2.5 mM KCl, 10 mM MgCl₂, 10 mM MgSO₄ and 20 mM glucose) at 37°C with shaking for 1 hour. Samples are then spread onto LB (10 g/l bacto tryptone, 5 g/l bacto yeast extract, 10 g/l sodium chloride) plates containing 100 microgram/ml of Ampicillin, 0.3% X-gal, and 100 microgram/ml IPTG. These plates are incubated overnight at 37°C. Ampicillin-resistant colonies with white color are selected, grown in 5 ml of liquid LB containing 100 microgram/ml of Ampicillin, and plasmid DNA is isolated using the Qiagen miniprep protocol (Qiagen, Gaithersburg, MD, USA).

To verify that the correct *H.pylori* DNA inserts had been cloned, these pT7Blue plasmid DNAs are used as templates for PCR amplification of the cloned inserts, using the same forward and reverse primers used for the initial amplification of the J99 *H.pylori* sequence. Recognition of the primers and a PCR product of the correct size as visualized on a 2% TAE, ethidium bromide stained agarose gel are confirmation that the correct inserts had been cloned. Two to six such verified clones are obtained for each knock-out target, and frozen at -70°C for storage. To minimize errors due to PCR, plasmid DNA from these verified clones are pooled, and used in subsequent cloning steps.

The sequences of the genes/ORFs are again used to design a second pair of primers which flank the region of *H. pylori* DNA to be either interrupted or deleted (up to 250 basepairs) within the ORFs but are oriented away from each other. The pool of

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circular plasmid DNAs of the previously isolated clones are used as templates for this round of PCR. Since the orientation of amplification of this pair of deletion primers is away from each other, the portion of the ORF between the primers is not included in the resultant PCR product. The PCR product is a linear piece of DNA with *H. pylori* DNA at each end and the pT7Blue vector backbone between them which, in essence, resultes in the deletion of a portion of the ORFs. The PCR product is visualized on a 1% TAE, ethidium bromide stained agarose gel to confirm that only a single product of the correct size has been amplified.

A Kanamycin-resistance cassette (Labigne-Roussel et al., 1988 J. Bacteriology 170, 1704-1708) is ligated to this PCR product by the TA cloning method used 10 previously (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994). The Kanamycin cassette containing a Campylobacter kanamycin resistance gene is obtained by carrying out an EcoRI digestion of the recombinant plasmid pCTB8:kan (Cover et al., 1994, J. Biological Chemistry 269, pp. 10566-10573). The proper fragment (1.4 kb) is isolated on a 1% TAE gel, and isolated 15 using the QIAquick gel extraction kit (Qiagen, Gaithersburg, MD, USA). The fragment is end repaired using the Klenow fill-in protocol, which involved mixing 4ug of the DNA fragment, 1 microliter of dATP,dGTP, dCTP, dTTP at 0.5 mM, 2 microliter of Klenow Buffer (New England Biolabs) and 5 units of Klenow DNA Polymerase I Large (Klenow) Fragment (New England Biolabs) into a 20 microliter reaction, incubating at 20 30°C for 15 min, and inactivating the enzyme by heating to 75°C for 10 minutes. This blunt-ended Kanamycin cassette is then purified through a Qiaquick column (Qiagen, Gaithersburg, MD, USA) to eliminate nucleotides. The "T" overhang is then generated by mixing 5 micrograms of the blunt-ended kanamycin cassette, 10 mM Tris pH 8.3, 50 mM KCl, 2 mM MgCl₂, 5 units of DNA Polymerase (Amplitaq, Roche Molecular 25 Systems, Inc., Branchburg, NJ, USA), 20 microliters of 5 mM dTTP, in a 100 microliter reaction and incubating the reaction for 2 hours at 37°C. The "Kan-T" cassette is purified using a QIAquick column (Qiagen, Gaithersburg, MD, USA). The PCR product of the deletion primers (F2 and R2) is ligated to the Kan-T cassette by mixing 10 to 25 ng of deletion primer PCR product, 50 - 75 ng Kan-T cassette DNA, 1 30 microliter 10x T4 DNA Ligase reaction mixture, 0.5 microliter T4 DNA Ligase (New England Biolabs, Beverly, MA, USA) in a 10 microliter reaction and incubating for 16 hours at 16°C.

The ligation products are transformed into XL-1 Blue or DH5-a *E.coli* cells by electroporation as described previously. After recovery in SOC, cells are plated onto LB plates containing 100 microgram/ml Ampicillin and grown overnight at 37°C. These plates are then replica plated onto plates containing 25 microgram/ml Kanamycin and

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allowed to grow overnight. Resultant colonies have both the Ampicillin resistance gene present in the pT7Blue vector, and the newly introduced Kanamycin resistance gene. Colonies are picked into LB containing 25 microgram/ml Kanamycin and plasmid DNA is isolated from the cultured cells using the Qiagen miniprep protocol (Qiagen, Gaithersburg, MD, USA).

Several tests by PCR amplification are conducted on these plasmids to verify that the Kanamycin is inserted in the H. pylori gene/ORF, and to determine the orientation of the insertion of the Kanamycin-resistance gene relative to the H. pylori gene/ORF. To verify that the Kanamycin cassette is inserted into the H. pylori sequence, the plasmid DNAs are used as templates for PCR amplification with the set of primers originally used to clone the H. pylori gene/ORFs. The correct PCR product is the size of the deleted gene/ORF but increased in size by the addition of a 1.4 kilobase Kanamycin cassette. To avoid potential polar effects of the kanamycin resistance cassette on H. pylori gene expression, the orientation of the Kanamycin resistance gene with respect to the knock-out gene/ORF is determined and both orientations are eventually used in H. pylori transformations (see below). To determine the orientation of insertion of the kanamycin resistance gene, primers are designed from the ends of the kanamycin resistance gene ("Kan-1" 5'-ATCTTACCTATCACCTCAAAT-3' (SEQ ID NO:207)), and "Kan-2" 5'-AGACAGCAACATCTTTGTGAA-3' (SEQ ID NO:208)). By using each of the cloning primers in conjunction with each of the Kan primers (4 combinations of primers), the orientation of the Kanamycin cassette relative to the H.pylori sequence is determined. Positive clones are classified as either in the "A" orientation (the same direction of transcription is present for both the H. pylori gene and the Kanamycin resistance gene), or in the "B" orientation (the direction of transcription for the H.pylori gene is opposite to that of the Kanamycin resistance gene). Clones which share the same orientation (A or B) are pooled for subsequent experiments and independently transformed into H. pylori.

Transformation of Plasmid DNA into H. pylori cells

Two strains of *H. pylori* are used for transformation: ATCC <u>55679</u>, the clinical isolate which provided the DNA from which the *H. pylori* sequence database is obtained, and AH244, an isolate which had been passaged in, and has the ability to colonize the mouse stomach. Cells for transformation are grown at 37°C, 10% CO₂, 100% humidity, either on Sheep-Blood agar plates or in Brucella Broth liquid. Cells are grown to exponential phase, and examined microscopically to determine that the cells are "healthy" (actively moving cells) and not contaminated. If grown on plates, cells are harvested by scraping cells from the plate with a sterile loop, suspended in 1 ml of

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Brucella Broth, spun down (1 minute, top speed in eppendorf microfuge) and resuspended in 200 microliters Brucella Broth. If grown in Brucella Broth liquid, cells are centrifuged (15 minutes at 3000 rpm in a Beckman TJ6 centrifuge) and the cell pellet resuspended in 200 microliters of Brucella broth. An aliquot of cells is taken to determine the optical density at 600 nm, in order to calculate the concentration of cells. An aliquot (1 to 5 OD₆₀₀ units/25 microliter) of the resuspended cells is placed onto a prewarmed Sheep-Blood agar plate, and the plate is further incubated at 37°C, 6% CO₂, 100% humidity for 4 hours. After this incubation, 10 microliters of plasmid DNA (100 micrograms per microliter) is spotted onto these cells. A positive control (plasmid DNA with the ribonuclease H gene disrupted by kanamycin resistance gene) and a negative control (no plasmid DNA) are done in parallel. The plates are returned to 37°C, 6% CO₂ for an additional 4 hours of incubation. Cells are then spread onto that plate using a swab wetted in Brucella broth, and grown for 20 hours at 37°C, 6% CO₂. Cells are then transferred to a Sheep-Blood agar plate containing 25 micrograms/ml Kanamycin, and allowed to grow for 3 to 5 days at 37°C, 6% CO₂, 100% humidity. If colonies appear, they are picked and regrown as patches on a fresh Sheep-Blood agar plate containing 25 micrograms/ml Kanamycin.

Three sets of PCR tests are done to verify that the colonies of transformants have arisen from homologous recombination at the proper chromosomal location. The template for PCR (DNA from the colony) is obtained by a rapid boiling DNA preparation method as follows. An aliquot of the colony (stab of the colony with a toothpick) is introduced into 100 microliters of 1% Triton X-100, 20 mM Tris, pH 8.5, and boiled for 6 minutes. An equal volume of phenol: chloroform (1:1) is added and vortexed. The mixture is microfuged for 5 minutes and the supernatant is used as DNA template for PCR with combinations of the following primers to verify homologous recombination at the proper chromosomal location.

TEST 1. PCR with cloning primers originally used to amplify the gene/ORF. A positive result of homologous recombination at the correct chromosomal location should show a single PCR product whose size is expected to be the size of the deleted gene/ORF but increased in size by the addition of a 1.4 kilobase Kanamycin cassette. A PCR product of just the size of the gene/ORF is proof that the gene had not been knocked out and that the transformant is not the result of homologous recombination at the correct chromosome location.

TEST 2. PCR with F3 (primer designed from sequences upstream of the gene/ORF and not present on the plasmid), and either primer Kan-1 or Kan-2 (primers designed from the ends of the kanamycin resistance gene), depending on whether the plasmid DNA used was of "A" or "B" orientation. Homologous recombination at the

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correct chromosomal location will result in a single PCR product of the expected size (i.e., from the location of F3 to the insertion site of kanamycin resistance gene). No PCR product or PCR product(s) of incorrect size(s) will prove that the plasmid had not integrated at the correct site and that the gene had not been knocked out.

TEST 3. PCR with R3 (primer designed from sequences downstream of the gene/ORF and not present on the plasmid) and either primer Kan-1 or Kan-2, depending on whether the plasmid DNA used was of "A" or "B" orientation. Homologous recombination at the correct chromosomal location will result in a single PCR product of the expected size (i.e., from the insertion site of kanamycin resistance gene to the downstream location of R3). Again, no PCR product or PCR product(s) of incorrect size(s) will prove that the plasmid had not integrated at the correct site and that the gene had not been knocked out.

Transformants showing positive results for all three tests above indicate that the gene is not essential for survival *in vitro*.

A negative result in any of the three above tests for each transformant indicates that the gene had not been disrupted, and that the gene is essential for survival in vitro.

In the event that no colonies result from two independent transformations while the positive control with the disrupted ribonuclease H plasmid DNA produces transformants, the plasmid DNA is further analyzed by PCR on DNA from transformant populations prior to plating for colony formation. This will verify that the plasmid can enter the cells and undergo homologous recombination at the correct site. Briefly, plasmid DNA is incubated according to the transformation protocol described above. DNA is extracted from the *H. pylori* cells immediately after incubation with the plasmid DNAs and the DNA is used as template for the above TEST 2 and TEST 3. Positive results in TEST 2 and TEST 3 would verify that the plasmid DNA could enter the cells and undergo homologous recombination at the correct chromosomal location. If TEST 2 and TEST 3 are positive, then failure to obtain viable transformants indicates that the gene is essential, and cells suffering a disruption in that gene are incapable of colony formation

VII. High-throughput drug screen assay

Cloning, expression and protein purification

Cloning, transformation, expression and purification of the *H. pylori* target gene and its protein product, e.g., an *H. pylori* enzyme, to be used in a high-throughput drug screen assay, is carried out essentially as described in Examples II and III above. Development and application of a screening assay for a particular *H. pylori* gene product, peptidyl-propyl *cis-trans* isomerase, is described below as a specific example.

Enzymatic Assay

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The assay is essentially as described by Fisher (Fischer, G., et.al. (1984) *Biomed. Biochim. Acta* 43:1101-1111). The assay measures the *cis-trans* isomerization of the Ala-Pro bond in the test peptide N-succinyl-Ala-Ala-Pro-Phe-p-nitroanilide (Sigma # S-7388, lot # 84H5805). The assay is coupled with α-chymotrypsin, where the ability of the protease to cleave the test peptide occurs only when the Ala-Pro bond is in *trans*. The conversion of the test peptide to the trans isomer in the assay is followed at 390 nm on a Beckman Model DU-650 spectophotometer. The data are collected every second with an average scanning of time of 0.5 second. Assays are carried out in 35 mM Hepes, pH 8.0, in a final volume of 400 ul, with 10 μM α-chymotrypsin (type 1-5 from bovine Pancreas, Sigma # C-7762, lot 23H7020) and 10 nM PPIase. To initiate the reaction, 10 μl of the substrate (2 mM N-Succinyl-Ala-Ala-Pro-Phe-p-nitroanilide in DMSO) is added to 390 μl of reaction mixture at room temperature.

15 Enzymatic assay in crude bacterial extract.

A 50 ml culture of *Helicobacter pylori* (strain J99) in Brucella broth is harvested at mid-log phase (OD $_{600~nm} \sim 1$) and resuspended in lysis buffer with the following protease inhibitors: 1 mM PMSF, and 10 μ g/ml of each of aprotinin, leupeptin, pepstatine, TLCK, TPCK, and soybean trypsin inhibitor. The suspension is subjected to 3 cycles of freeze-thaw (15 minutes at -70 °C, then 30 minutes at room temperature), followed by sonication (three 20 second bursts). The lysate is centrifuged (12,000 g x 30 minutes) and the supernatant is assayed for enzymatic activity as described above.

Many *H. pylori* enzymes can be expressed at high levels and in an active form in *E. coli*. Such high yields of purified proteins provide for the design of various high throughput drug screening assays.

EQUIVALENTS

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments and methods described herein. Such equivalents are intended to be encompassed by the scope of the following claims.

SEQUENCE LISTING

	1) GENERAL INFORMATION:
5	
_	(4) 2007 7027
	(i) APPLICANT:
	(A) NAME: Astra Aktiebolag
	(B) STREET: S-151 85
•	(C) CITY: Sodertalje
10	(D) STATE:
	(E) COUNTRY: Sweden
	(F) POSTAL CODE (ZIP)
	(ii) TITLE OF INVENTION: NUCLEIC ACID AND AMINO ACID SEQUENCES
15	RELATING TO HELICOBACTER PYLORI AND
	VACCINE COMPOSITIONS THEREOF
	(iii) NUMBER OF SEQUENCES: 208
20	(111) NOTABLE OF BEGGENCES. 200
20	· · · · · · · · · · · · · · · · · · ·
	(iv) COMPUTER READABLE FORM:
	(A) MEDIUM TYPE:
	(B) COMPUTER:
	(C) OPERATING SYSTEM:
25	(D) SOFTWARE:
	(v) CURRENT APPLICATION DATA:
•	(A) APPLICATION NUMBER
30	(B) FILING DATE:
30	
	(vi) PRIOR APPLICATION DATA:
	(A) APPLICATION NUMBER:US 08/739,150
	(B) FILING DATE: 28-OCT-1996
35	(vii) PRIOR APPLICATION DATA:
,	(A) APPLICATION NUMBER: US 08/759,739
	(B) FILING DATE: 06-DEC-1996
	(2) IIIING DAIL. 00-DEC-1996
	(viii) PRIOR APPLICATION DATA:
40	
40	(A) APPLICATION NUMBER: US 08/891,928
	(B) FILING DATE: 14-JULY-1997
	(ix) CORRESPONDENCE ADDRESS:
	(A) ADDRESSEE: LAHIVE & COCKFIELD
45	(B) STREET: 28 State Street
	(C) CITY: Boston
	(D) STATE: Massachusetts
•	
	(E) COUNTRY: USA
	(F) ZIP: 02109-1875
50	
	(x) ATTORNEY/AGENT INFORMATION:
	(A) NAME: Mandragouras, Amy E.
	(B) REGISTRATION NUMBER: 36,207
	(C) REFERENCE/DOCKET NUMBER: GTN-001CP10PC
55	(a)

```
(xi) TELECOMMUNICATION INFORMATION:
                (A) TELEPHONE: (617)227-7400
                (B) TELEFAX: (617) 742-4214
      (2) INFORMATION FOR SEQ ID NO:1:
           (i) SEQUENCE CHARACTERISTICS:
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20	(C) STRANDEDNESS: double	
20	(D) TOPOLOGY: circular	
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20	(A) ORGANISM: Helicobacter pylori	
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	(2) 20011101 12030	
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PCT/US97/19575

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WO 98/18323

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               (C) STRANDEDNESS: double
               (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
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        (iii) HYPOTHETICAL: NO
        (iv) ANTI-SENSE: NO
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         (vi) ORIGINAL SOURCE:
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50 (iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

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	(vi) ORIGINAL SOURCE:	
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	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:	•
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1368

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(2) INFORMATION FOR SEQ ID NO:8: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 849 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular 10 (ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO 15 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori 20 (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1...849 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8: 25 ATGGGGTGTT CGTTTATCTT TAAAAAAGTT AGGGTTTATT CTAAAATGTT GGTTGCTTTG GGGCTTTCAA GCGTGTTGAT CGGTTGCGCG ATGAATCCAA GCGCTGAGAC AAAAAAACCA 120 AATGACGCCA AAAACCAACA ACCAGTTCAA ACTCATGAAA GAATGACAAC AAGTTCTGAA 180 CATGTTACGC CACTAGATTT TAATTACCCG GTGCATATTG TTCAAGCCCC ACAAAACCAT 240 CATGTTGTAG GTATTTTAAT GCCACGCATT CAAGTGAGCG ATAATCTAAA ACCCTATATT 300 GATAAGTITC AAGACGCTTT AATTAATCAA ATCCAAACTA TTTTTGAAAA AAGAGGCTAT 360 CAAGTGTTGC GTTTTCAAGA TGAAAAAGCT TTGAATGTGC AAGATAAGAA AAAGATTTTT 420 TCCGTTTTGG ATTTGAAAGG GTGGGTAGGA ATCTTAGAAG ATTTGAAAAT GAATTTAAAA 480 GATCCCAATA GTCCCAATTT AGACACGCTA GTGGATCAAA GCTCAGGCTC TGTATGGTTT 540 AATTTTTATG AACCAGAAAG CAATCGTGTC GTCCATGATT TTGCTGTAGA AGTAGGAACT TTTCAGGCAA TAACATACAC ATACACCTCT ACTAATAACG CTTCAGGAGG GTTTAATTCT 660 TCAAAAAGCG TTATCCATGA AAATTTGGAT AAGAATAGAG AAGACGCGAT ACACAAGATT 720 TTAAACAGAA TGTATGCGGT TGTCATGAAA AAAGCTGTAA CAGAACTTAC AAAAGAAAAT 780 ATCGCCAAAT ACAGAGACGC TATTGATAGA ATGAAAGGCT TTAAAAGTTC TATGCCTCAA 840 40 AAAAAGTAG 849 (2) INFORMATION FOR SEQ ID NO:9: (i) SEQUENCE CHARACTERISTICS: 45 (A) LENGTH: 843 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular .50 (ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

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    AATCCCAACA ACAAAGAAAA ACCACAGACC TTTGATGTGT TGCAAGGAAG TCAGCCAATG
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    GTGATCAATG AAGTGGCAAG AGAAAAAGCT CAGCTAGAAA AAATCAATCA GTATTACAAG
                                                                      600
20
    ACTCTCTTGC AAGACAAGGA ACAAGAATAT ACCACTAGGA AAAATAACCA ACGAGAAATT
                                                                      660
    TTAGAAACAT TGAGTAATCG TGCAGGTTAT CAAATGAGGC AGAATGTGAT TAGTTCTGAG
                                                                      720
    ATTTTTAAGA ATGGCAACTT GAACATGCAA GCCAAAGAAG AAGAAGTTAG GGAGAAGCTA
    840
                                                                      843
25
     (2) INFORMATION FOR SEQ ID NO:10:
         (i) SEQUENCE CHARACTERISTICS:
              (A) LENGTH: 1179 base pairs
30
              (B) TYPE: nucleic acid
              (C) STRANDEDNESS: double
              (D) TOPOLOGY: circular
        (ii) MOLECULE TYPE: DNA (genomic)
35
       (iii) HYPOTHETICAL: NO
        (iv) ANTI-SENSE: NO
40
        (vi) ORIGINAL SOURCE:
              (A) ORGANISM: Helicobacter pylori
        (ix) FEATURE:
              (A) NAME/KEY: misc feature
45
              (B) LOCATION 1...1179
        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:
    ATGAGAAAAC TATTCATCCC ACTTTTATTA TTCAGCGCTT TAGAAGCGAA CGAGAAAAAC
    GGCTTTTTCA TAGAAGCCGG CTTTGAAACT GGGCTATTAG AAGGCACACA AACGCAAGAA
    AAAAGACACA CCACCACAAA AAACACTTAC GCAACTTACA ATTATTTACC CACAGACACG
    ATTTTAAAAA GAGCGGCTAA TTTATTCACC AATGCCGAAG CGATTTCAAA ATTAAAATTC 240
    TCATCTTTAT CCCCTGTTAG AGTGTTGTAT ATGTATAATG GTCAATTAAC TATAGAAAAC
                                                                      300
    TTCTTGCCTT ATAATTTAAA TAATGTTAAG CTTAGTTTTA CAGACGCTCA AGGCAATGTG
                                                                      360
  ATCGATCTAG GCGTGATAGA GACTATCCCC AAACACTCTA AGATTGTTTT GCCCGGAGAG
```

	GCATTTGATA GTCTAAAAAT TGACCCCTAT ACTTTATTTC TTCCAAAAAT TGAAGCCACT	480
	AGCACTTCTA TTTCTGACGC TAACACGCAG AGGGTGTTTG AAACGCTCAA TAAGATTAAG	540
	ACAAATTTGG TCGTAAATTA TAGGAATGAA AACAAATTTA AAGATCACGA AAATCATTGG	600
_	GAAGCCTTTA CCCCACAAAC CGCAGAAGAA TTCACTAATT TAATGTTGAA CATGATCGCT	660
.5	GTTTTAGACT CCCAATCTTG GGGCGATGCG ATCTTAAACG CTCCTTTTGA GTTCACTAAC	720
-	AGCCCAACAG ATTGCGATAA TGATCCTTCA AAATGCGTAA ATCCTGGGAC AAACGGGCTT	780
	GTCAATTCTA AAGTCGATCA AAAATATGTG TTAAACAAAC AAGACATTGT CAATAAATTT	840
	AAAAACAAAG CGGATCTTGA TGTAATTGTT TTAAAGGATT CAGGGGTTGT AGGGCTTGGG	900
10	AGTGATATTA CCCCTAGCAA CAATGATGAT GGCAAGCATT ATGGCCAGTT AGGGGTAGTA	960
10	GCTTCTGCTT TAGATCCTAA AAAACTCTTT GGCGATAACC TTAAGACTAT CAATTTAGAG	1020
	GATTTAAGAA CCATCTTGCA TGAATTCAGC CACACTAAAG GCTATGGGCA TAACGGGAAT	1080
	ATGACCTATC AAAGAGTGCC GGTAACGAAA GATGGTCAAG TGGAAAAGGA TAGTAATGGC	1140
	AAGCCAAAAG ATTCTGATGG CCTCCCCTAT AATGTGTGT	1179
15	(A) TURONUMTON TOP OTO TO NO	
13	(2) INFORMATION FOR SEQ ID NO:11:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 813 base pairs	
	(B) TYPE: nucleic acid	
20	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
	(2)	
	(ii) MOLECULE TYPE: DNA (genomic)	
~ ~		
25	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
30		
50	(A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	
	(A) NAME/KEY: misc feature	
	(B) LOCATION 1813	
35		
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:	
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	GAAGGTGATG GTGTTTATAT AGGGACTAAT TATCAGCTTG GACAAGCCCG TTTGAATAGC	120
40	AATATTTATA ATACAGGGGA TTGCACAGGG AGTGTTGTAG GTTGCCCCCC AGGTCTTACC	180
	GCTAATAAGC ATAATCCAGG AGGCACCAAT ATCAATTGGC ACTCCAAATA CGCTAATGGG	240
	GCTTTGAATG GTTTTGGGTT GAATGTGGGT TATAAGAAAT TCTTCCAATT CAAGTCGCTA	300
	GATATGACAA GCAAGTGGTT TGGTTTTAGA GTGTATGGGC TTTTTGATTA CGGGCATGCC	360
	GATTTAGGTA AACAAGTTTA TGCACCTAAT AAAATCCAGT TGGATATGGT CTCTTGGGGT	420
45	GTGGGGAGCG ATTTGTTAGC TGATATTATT GATAAAGACA ACGCTTCTTT TGGTATTTTT	480
	GGTGGGGTCG CTATCGGCGG TAACACTTGG AAAAGCTCTG CAGCAAACTA TTGGAAAGAG	540
	CAAATCATTG AAGCCAAAGG TCCTGATGTT TGTACCCCTA CTTATTGTAA CCCTAATGCC	600
	CCTTATAGCA CCAACACTTC AACCGTCGCT TTTCAAGTGT GGTTGAATTT TGGGGTGAGA	660
	GCCAATATCT ACAAGCATAA TGGCGTGGAA TTTGGCGTGA GAGTGCCGCT ACTCATCAAT	720
50	AAATTTTTGA GCGCGGGTCC TAACGCTACT AACCTTTATT ACCATTTGAA ACGGGATTAT	780
	TCGCTTTATT TGGGGTATAA CTACACTTTT TAA	813
	(2) INFORMATION FOR SEQ ID NO:12:	

_	(A) LENGTH: 423 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: double(D) TOPOLOGY: circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
10	(iv) ANTI-SENSE: NO	
	<pre>(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori</pre>	
15	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1423</pre>	
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:	. •
20	ATGCATCCTA TAATGTTTGC CTATATCGCT AACGCGCTCG CTCAAGCTAG AAAGATCAAC GGAACACTTT GCATGGCGTT TCAAAAAATA TCTCAAGTCA AAGAATTAGG CATTGATAAA GCAAAGAGTT TGATAGGCAA CCTTTCTCAA GTGATTATCT ACCCCACAAA AGATACTGAT GAATTAATAG AATGTGGCGT CCCATTAAGC GATAGTGAAA TCAATTTCTT ACACAACACG	120 180 240
25	GAATTAATAG AATGIGGGGT CCCATTAAGC GATAGIGAAA TCAATTCTT ACACTTTATT GAAATTGATT TAAAAAAGAT TTGCAAGAAC TACTTTATAT TCTTGATAGC AATGCTGGTA ATAGAAAAAT CCTCAATGAT CTTAAAAAAG CAAACCAAGA AACTTATAAG GAAGAGTATT TAA	300 360 420 421
30	(2) INFORMATION FOR SEQ ID NO:13:	
35	(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 771 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: double(D) TOPOLOGY: circular	-
	(ii) MOLECULE TYPE: DNA (genomic)	
40	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
45	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1771</pre>	
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:	
55	ATGTTGGGGA GCGTCAAAAA AGCGGTTTTT AGGGTTTTGT GTTTGGGGGC GTTGTGTTTA TGCGGGGGGT TAATGGCAGA GCAAGATCCT AAAGAGCTTA TATTTTCAGG TATAACTATT TACACGGATA AAAATTTCAC TAGAGCTAAG AAATATTTTG AAAAAGCTTG CAAATCAAAC	6 12 18

	GATGCTGATG GCTGTGCAAT CTTAAGAGAG GTTTATTCTA GTGGTAAAGC CATAGCGAGA	240
	GAAAACGCAA GAGAGAGCAT TGAAAAAGCT CTTGAACACA CCGCTACTGC TAAAGTTTGT	300
	AAATTAAACG ATGCTGAAAA ATGCAAGGAC TTAGCAGAGT TTTATTTTAA TGTAAACGAT	360
	CTTAAAAATG CTTTAGAATA TTACTCTAAA TCTTGTAAGT TAAATAATGT TGAAGGGTGT	420
5	ATGCTGTCAG CAACTTTTTA TAACGATATG ATAAAGGGTT TGAAAAAAGA TAAAAAAGAT	480
	CTAGAATATT ATTCTAAAGC TTGCGAGTTA AATAACGGTG GAGGGTGTTC TAAATTAGGA	540
	GGGGATTATT TTTTTGGTGA AGGCGTAACA AAAGATTTCA AAAAAGCTTT TGAATATTCT	600
	GCCAAAGCTT GTGAGTTGAA CGATGCTAAA GGGTGTTACG CTCTAGCAGC GTTTTATAAT	660
	GAGGGTAAAG GCGTGGCAAA GGATGAAAAG CAAACGACAG AAAACCTTGA AAAGAGTTGC	720
10	AAGCTAGGAT TAAAAGAAGC ATGCGATATT CTCAAAGAAC AAAAACAATA A	771
	(2) INFORMATION FOR SEQ ID NO:14:	
·	(i) SEQUENCE CHARACTERISTICS:	
15	(A) LENGTH: 729 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
*	(D) TOPOLOGY: circular	
20	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
25		
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	
30	(A) NAME/KEY: misc_feature	
	(B) LOCATION 1729	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:	
35		
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	CATGCGGATA TTAATTCTCA AAAACAAGCC ACCAACGCTA CGATCAAAGG CTTTGACGCG	180
	CTCTTGGGGT ATCAATTTT CTTTGAAAAA CACTTTGGCT TACGCCTTTA TGGGTTTTTT	240
40	GACTACGCTC ATGCCAATTC TATTAAGCTT AAAAACCCTA ACTATAATAG CGAAGCGGCG	300
ŧU	CAAGTGGCTA GTCAAATTCT TGGGAAACAA GAAATCAATC GTTTAACAAA CATTGCCGAT	360
	CCCAGAACTT TTGAGCCGAA CATGCTCACT TATGGGGGGG CTATGGACGT GATGGTTAAT	420
	GTCATCAATA ACGGCATCAT GAGTTTGGGG GCTTTTGGCG GGATACAATT GGCCGGCAAT	480
	TCATGGCTTA TGGCGACACC GAGCTTTGAG GGCATTTTAG TGGAACAAGC CCTTGTGAGC	
15	AAGAAAGCCA CTTCTTTCCA ATTTTTATTC AATGTGGGGG CTCGCTTAAG GATCTTAAAA	600
+3	CATTCTAGCA TTGAAGCGGG CGTGAAATTC CCCATGCTAA AGAAAAACCC CTACATCACT	660
	GCAAAAATT TGGATATAGG GTTTAGGCGC GTGTATTCGT GGTATGTGAA TTACGTGTTC	720
	ACTTTCTAG	729
	(2) INFORMATION FOR SEQ ID NO:15:	
50	(;) CEOUTINGE GUADAGEERTORTOG	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 804 base pairs	
	(B) TYPE: nucleic acid	
55	(C) STRANDEDNESS: double	
, ,	. CON TOPONARY CONTROLLAR	

	(ii) MOLECULE TYPE: DNA (genomic)	
5	(iii) HYPOTHETICAL: NO	
3	(iv) ANTI-SENSE: NO	
* *.	(vi) ORIGINAL SOURCE:	
10	(A) ORGANISM: Helicobacter pylori	
	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1804</pre>	
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:	
20	ATGAACTACC CTAATCTACC TAACAGCGCT TTAGAGATAA GCGAACAGCC AGAAGTGAAA GAAATCACTA ACGAGCTTT AAAGCAATTA CAAAACGCTT TAAGGAGCAA CGCGCATTTT AGCGAGCAAG TGGAATTAAG CCTTAAATGC ATCGTTAGGA TTTTAGAAGT GCTTTTGAGT TTGGATTTTT TTAAGAATGC GAATGAGATT GATAGCAGTT TAAGAAATTC CATTGAGTGG CTGACTAACG CCGGCGAGAG CTTGAAATTA AAAATGAAAG AATACGAGCG CTTTTTTAGC GAGTTTAATA CGAGCATGCA TGCCAACGAG CAGGAAGTAA CCAATACCTT AAACGCTAAC	120 180 240 300 360
25	GCCGAGAACA TTAAAAGCGA AATTAAAAAG CTAGAAAATC AATTGATAGA AACCACGACA AGACTTTTAA CGAGCTATCA AATCTTTTTA AACCAAGCCA GAGATAACGC TAACAACCAA ATCACAAAAA ACAAAACCCA AAGCCTTGAA GCGATTACAC AAGCTAAAAA CAACGCTAAT AATGAAATAA GCAACAATCA AACGCAAGCG ATAACTAATA TCACCGAAGC GAAAACGAAC GCTAATAATG AAATAAGCAA CAATCAAACG CAAGCGATAA CTAACATTAA CGAAGCCAAA	426 486 546 606
30	GAAAGCGCTA CAACGCAAAT AAACGCCAAT AAGCAAGAAG CAATAAATAA CATCACGCAA GAAAAAAACCC AAGCCACAAG CGAGATCACC GAAGCGAAAA AGACCGATCA TTATCAAAAC	720 780
,0	(2) INFORMATION FOR SEQ ID NO:16:	804
35	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1632 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular	
10	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
15	<pre>(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:</pre>	
	(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 11632	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:	
5	GTGATAGAGA CCATCCCCAA ACACTCTAAG ATTGTTTTAC CCGGGGAGGC GTTTGATAGT	60

	TTAAAAGAGG CGTTTGATAA AATTGACCCC TATACTTTCT TTTTTCCAAA ATTTGAAGCC	100
	ACTAGCACTT CTATTTCTGA TACTAACACG CAGAGGGTGT TTGAAACGCT CAATAACATT	120
	ΔΔΔΔΓΔΔΔΓΓ ΤΤΔΤΑΤΓΙΛ ΑΤΑΤΡΑΤΡΑΤΡΑΤΡΑΤΡΑΤΡΑΤΡΑΤΡΑΤΡΑ	180
	TACAATAATA ATGGTAATAC AAAAAMGAM MOMMOGGAAA	240
5	GAAGAATTCA CCAATTTAAT CTTCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAGATCAAG	300
	GATGCGATCT TAAACGCTCC TTTTCAATTC ACTAACAT CACCA CAACAA	360
	CCTTCAAAAT GCGTAAATCC CCCACTAAAT GGGGGGGGGG	420
	ΤΆΤΑΤΑΓΤΟΝ ΑΓΑΛΟΛΑΓΟ ΤΑΡΤΑΤΙΚΑΝ ΑΝΙΜΙΚΑΝΑ ΑΝΙΜΙΚΑΝΑ ΑΝΙΜΙΚΑΝΑ ΑΝΙΜΙΚΑΝΑ ΑΝΙΜΙΚΑΝΑ ΑΝΙΜΙΚΑΝΑ ΑΝΙΜΙΚΑΝΑ ΑΝΙΜΙΚΑΝΑ	480
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10	TATGGCACAT TAGGGGTAGA AGCCTATGCT TTAGATCCTA AAAAACTCTT TGGCAACGAC	600
••	CTTAAGACTA TCAATTTAGA AGCCTATAGA ACCATCTTGC ATGAATTCAG CCACACTAAA	660
	GGCTATGGGC ATAACGGAA TATGAGGGTAT GAAAGAGTCTGC ATGAATTCAG CCACACTAAA	720
	GGCTATGGGC ATAACGGGAA TATGACCTAT CAAAGAGTGC CGGTAACGAA AGATGGTCAA	780
	GTGGAAAAGG ATAGTAATGG CAAGCCAAAA GATTCTGATG GCCTCCCCTA TAATGTGTGT	840
15	TCGCTTTATG GGGGATCCAA TCAGCCCGCT TTCCCTAGCA ACTACCCTAA TTCCATCTAT	900
	CACAATTGTG CGGATGTCCC GGCTGGCTTT TTAGGGGGTAA CAGCAGCGGT TTGGCAGCAG	960
	CTCATCAATC AAAACGCCTT GCCGATCAAC TACGCTAACT TGGGGAGTCA AACAAACTAC 1	020
	AACCTAAACG CTAGTTTAAA CACGCAAGAT TTAGCCAATT CCATGCTCAG CACCATCCAA 1	080
	AAAACCTTTG TAACTTCTAG CGTTACCAAC CACCATTTTT CAAACGCATC GCAAAGTTTT 1	140
20	AGAAGCCCTA TTTTAGGGGT TAACGCTAAA ATAGGCTATC AAAACTACTT TAATGATTTC 1	200
20	ATAGGGTTGG CTTATTATGG CATCATCAAA TACAATTACG CTAAAGCTGT TAATCAAAAA 1	260
	GTCCAGCAAT TGAGCTATGG TGGGGGGATA GATTTGTTAT TGGATTTCAT CACCACTTAC 1	320
	TCCAATAAAA ATAGCCCTAC AGGCATTCAA ACCAAAAGGA ATTTTTCTTC ATCTTTTGGT 1	380
	ATCTTTGGGG GGTTAAGGGG CTTGTATAAC AGCTATTATG TGTTGAACAA AGTCAAAGGA 1	440
25	AGCGGCAATT TAGATGTGGC TACCGGGTTG AACTACCGCT ATAAGCATTC TAAATATTCT 1	500
23 .	GTAGGGATTA GCATCCCTTT AATCCAAAGA AAAGCTAGCG TCGTTTCTAG CGGTGGCGAT 1	560
	TATACGAACT CTTTTGTTTT CAATGAAGGG GCTAGCCACT TTAAGGTGTT TTTCAATTAC 10	620
	GGTGGGTGTT TT	532
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30	(2) INFORMATION FOR SEQ ID NO:17:	
30	(1)	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1071 base pairs	
	(B) TYPE: nucleic acid	
3.5	(C) STRANDEDNESS: double	
3.3	(D) TOPOLOGY: circular	
	(1)	
	(ii) MOLECULE TYPE: DNA (genomic)	
40	(iii) HYPOTHETICAL: NO	
40		
	(iv) ANTI-SENSE: NO	
•	(vi) ORIGINAL SOURCE:	
45	(A) ORGANISM: Helicobacter pylori	
45		
	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
	(B) LOCATION 11071	
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:	
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	ATCATTAAAA CGCAAAACGA TTTGTCCAAT GCCTGGTATC TCCCTCCACA AAAAGCCCCC 1	80
55	AAAGAACATT CTTGGGTGGA TTTTGCTAAA AAATATTTAA ACATGATGGA TTATCTAGGG	

AAAGAACATT CTTGGGTGGA TTTTGCTAAA AAATATTTAA ACATGATGGA TTATCTAGGC

960

	ACTTATTTTT TGCCTTTTTA TCATAGTTTC ACCCCCATTT TTCAATGGTA CCACCCTAAT	300
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	AGGCATATTC TTTGGACTAA AGGCACGCTT TATCTGGCTT ATACCCAAAC TAACTGGTTT	420
	CAAATTTATA ATGACCCTCA ATCCGCCCC ATGCGAATGA TCAATTTCAT GCCTGAACTC	480
5	ATCTATGTTT ATCCTATTAA TTTTAAACCT TTTGGGGGTA AAATAGGGAA TTTTTCTGAA	540
	ATTTGGATAG GTTGGCAGCA CATTTCTAAT GGTGTGGGGG GTGCGCAATG TTACCAGCCT	600
	TTTAATAAAG AAGGTAATCC TGAAAACCAG TTTCCAGGAC AACCTGTAAT CGTTAAAGAT	660
	TATAACGGGC AAAAAGATGT GCGCTGGGGG GGGTGTCKTT CGGTGARCSC GGGCAACSCC	720
	CTGTGTTTCG TTTTGGTGTG GGAAAAGGGA GGCCTAAAAA TCATGGTCGC TTATTGGCCC	780
10	TATGTCCCTT ATGATCAATC CAACCCTCAA TTGATTGATT ACATGGGGTA TGGTAACGCT	840
	AAAATTGATT ACAGGAGAGG GCGCCACCAT TTTGAATTGC AACTTTATGA TATTTTCACG	900
-	CAATACTGGC GTTATGATCG CTGGCATGGA GCTTTCCGCT TAGGCTATAC CTACCGCATT	960
	AACCCTTTTG TGGGGATTTA TGCGCAGTGG TTTAACGGCT ATGGCGATGG CTTGTATGAA	1020
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	(2) INFORMATION FOR SEQ ID NO:18:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 2028 base pairs	
20	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
	(b) Toronogi: Circular	
٥٢	(ii) MOLECULE TYPE: DNA (genomic)	
25	•	
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
30		
30	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	
25	(A) NAME/KEY: misc_feature	
35	(B) LOCATION 12028	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:	
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40	GTGTGCGTGA GCATTTTAGG GGTGTCCTTA AACAGCAGGG TGAAAGAGAT TTTAAAAGAA	120
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	TTGGAAAACA CTTATACGAG CATGGGCATT GTCAAAGAAA TGCTCCCTGA AGACACCAAA	240
•	AGAGAAATCA AAATCCAGTT GTTAAAAAAC TTCATTTTAG CCAATTCGCA TGTCGCTGGG	300
45	GTGAGCATGT TTTTTAAAGA CAGAGAGGAT TTGAGATTGA CGCTTTTACG AGATAACGAT	360
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	AAAAATAAAG AAATTTCTAA AAGCTTGCCT TATTACAGGA AAATGCCTAA CGGGGCGGAA	480
	GTTTATGGCG TGGATATTCT TTTACCACTA TTCAAGGAAA ACACGCAAGA AGTGGTGGGG	540
	GTTCTGATGA TTTTCTTTTC CATTGACAGC TTCAGTAATG AAATCACTAA AAACAGGAGC	600
66	GATTTATTTT TAATTGGCGT TAAAGGTAAA GTGCTTTTGA GCGCGAATAA AAGCTTGCAA	660
50	GACAAATCCA TCACCGAAAT TTATAAAAGC GTGCCTAAAG CCACTAATGA AGTGATGGCT	720
	ATTTTAGAAA ATGGCTCTAA AGCGACTTTA GAATACTTGG ATCCCTTTAG CCATAAGGAG	780
	AATTTTTTAG CCGTTGAAAC CTTTAAAATG CTAGGCAAAA CAGAAAGTAA AGACAATCTT	840
	AATTGGATGA TCGCTTTGAT CATTGAAAAA GACAAGGTCT ATGAGCAAGT GGGATCGGTG	900
	CCTTTTCTCC TCCTTCCACC CACTCCTATC AMCCTTCTTA CCTTTATA ACCTTTTCTC	

CGTTTTGTGG TGGTTGCAGC GAGTGCTATC ATGGTGTTAG CCTTAATCAT AGCGATCACT

CTTTTAATGC GAGCGATCGT GAGCAATCGT TTGGAAGTCG TTTCTAGCAC CTTGTCTCAT 1020

	•	
	TTCTTTAAAT TATTGAACAA TCAAGCCCAT TCTAGCGACA TTAAATTGGT TGAAGCGCGA	1080
	TCTAATGACG AATTAGGGCG CATGCAAACA GCGATCAATA AAAATATCTT GCAAACCCAA	1140
	AAAACCATGC AAGAAGACAG GCAAGCCGTC CAAGACACCA TTAAAGTGGT TTCAGACGTG	1200
	AAAGCGGGGA ATTTTGCGGT GCGCATCACG GCTGAACCCG CAAGCCCTGA TTTGAAAGAA	1260
5	TTGAGAGACG CGCTAAATGG GATCATGGAT TATTTGCAAG AAAGCGTAGG GACTCACATG	1320
-	CCAAGCATTT TCAAAATCTT TGAAAGCTAT TCTGGCTTGG ATTTTAGAGG GCGGATCCAA	1320
	AACGCTTCGG GTAGGGTGGA ATTGGTTACT AACGCTTTAG GGCAAGAAAT CCAAAAAATG	1380
	CTAGAAACTT CGTCTAATTT TGCCAAAGAT CTAGCGAACG ATAGCGCGAA TTTAAAAGAA	1440
	TGCGTGCAAA ATTTAGAAAA GGCTTCAAAC TCCCAACACA AAAGCCTGAT GGAAACTTCC	1500
10	AAAACGATAG AAAATATCAC CACTTCCATTT CAAACGCTTCA	
,	ATTGAACAAG GGAAAGACAT TAAAAGCATT GTAGAAATCA TTAGAGATAT TGCCGATCAA	1620
	ACGAATCTAT TAGCCCTAAA CGCTGCTATT GAAGCCGCAC GAGCCGGCGA GCATGGCAGA	
	GGCTTTGCGG TGGTGGCTGA TGAGGTGAGG AAGCTCGCTG AAAGGACGCA AAAATCCCTC	1740
•	AGTGAGATTG AAGCCAATAT TAATATTOOTH CONTROLLED AAAGGACGCA AAAATCCCTC	1800
15	AGTGAGATTG AAGCCAATAT TAATATTCTC GTTCAAAGCA TTTCAGACAC GAGCGAAAGC	1860
1.5	ATTAAAAACC AGGTTAAAGA AGTAGAAGAG ATCAACGCTT CTATTGAAGC CTTAAGATCG	1920
	GTTACTGAGG GCAATCTAAA AATCGCTAGC GATTCTTTAG AAATCAGTCA AGAAATTGAC	1980
	AAAGTCTCTA ACGATATTTT AGAAGATGTG AATAAAAAGC AGTTTTAA	2028
	(2)	
20	(2) INFORMATION FOR SEQ ID NO:19:	
20	(1)	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 816 base pairs	
	(B) TYPE: nucleic acid	
25	(C) STRANDEDNESS: double	
25	(D) TOPOLOGY: circular	
		*
•	(ii) MOLECULE TYPE: DNA (genomic)	
		• •
30	(iii) HYPOTHETICAL: NO	
30		
	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
35	(A) ORGANISM: Helicobacter pylori	
33		
	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
	(B) LOCATION 1816	
. 40		
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:	
	ATGAACATAT TCAAGCGTAT TATTTGCGTA ACCGCTATTG TTTTAGGTTT TTTTAACCTT	60
•	TIAGACGCCA AACACCACAA AGAAAAAAA GAAGACCACA AAATCACTCG TGAGCTTAAA	120
	GIGGGCGCTA ACCCTGTGCC GCATGCGCAA ATCTTGCAAT CAGTTGTGGA TGATTTGAAA	180
45	GAGAAAGGGA TCAAATTAGT GATCGTGTCT TTTACGGATT ATGTGTTGCC TAATTTAGCG	240
	CTCAATGACG GCTCTTTAGA CGCGAATTAC TTCCAGCACC GCCCTTATTT GGATCGGTTT	300
	AATTIGGACA GAAAAATGCA CCTTGTTGGT TTGGCCAATA TCCATGTGGA GCCTTTAAGA	360
	TTTTATTCTC AAAAAATCAC AGACATTAAA AACCTTAAAA AAGGCTCAGT GATTGCTGTG	420
	CCAAATGATC CGGCCAATCA AGGCAGGGCG TTGATTTTAC TCCATAACA AGGCCTTATC	
	GCTCTCAAAG ACCCAAGCAA TCTATACGCT ACGGAGTTTG ATATTGTCAA AAATCCTTAC	480
50	······································	540
50	AACATCAAAA TCAAACCCCT AGAAGCTGCG TTATTGCCTA AGCTTTTTACC COATGCTCA	
50	AACATCAAAA TCAAACCCCT AGAAGCTGCG TTATTGCCTA AGGTTTTAGG GGATGTGGAT	600
50	AACATCAAAA TCAAACCCCT AGAAGCTGCG TTATTGCCTA AGGTTTTAGG GGATGTGGAT GGGGCTATCA TAACAGGGAA TTATGCCTTG CAAGCAAAAC TCACCGGAGC CTTATTTTCA	600 660
50	AACATCAAAA TCAAACCCCT AGAAGCTGCG TTATTGCCTA AGGTTTTAGG GGATGTGGAT GGGGCTATCA TAACAGGGAA TTATGCCTTG CAAGCAAAAC TCACCGGAGC CTTATTTTCA GAAGATAAGG ACTCGCCTTA TGCTAATCTT GTAGCCTCTC GTGAGGATAA TGCGCAAGAT	600 660 720
55	AACATCAAAA TCAAACCCCT AGAAGCTGCG TTATTGCCTA AGGTTTTAGG GGATGTGGAT GGGGCTATCA TAACAGGGAA TTATGCCTTG CAAGCAAAAC TCACCGGAGC CTTATTTTCA GAAGATAAGG ACTCGCCTTA TGCTAATCTT GTAGCCTCTC GTGAGGATAA TGCGCAAGAT GAAGCGATAA AAGCGTTGAT TGAAGCCTTA CAGAGCGAAA AGACCAGGAA ATTCATTTTG	600 660 720 780
	AACATCAAAA TCAAACCCCT AGAAGCTGCG TTATTGCCTA AGGTTTTAGG GGATGTGGAT GGGGCTATCA TAACAGGGAA TTATGCCTTG CAAGCAAAAC TCACCGGAGC CTTATTTTCA GAAGATAAGG ACTCGCCTTA TGCTAATCTT GTAGCCTCTC GTGAGGATAA TGCGCAAGAT	600 660 720

	(2) INFO	RMATION FOR SEQ ID NO:20:
5	(i)	SEQUENCE CHARACTERISTICS:
)		(A) LENGTH: 486 base pairs
		(B) TYPE: nucleic acid (C) STRANDEDNESS: double
٠		(D) TOPOLOGY: circular
		(D) TOPOLOGI: CITCUIAL
0	(ii)	MOLECULE TYPE: DNA (genomic)
-	(iii)	HYPOTHETICAL: NO
5	(iv)	ANTI-SENSE: NO
,	(vi)	ORIGINAL SOURCE:
		(A) ORGANISM: Helicobacter pylori
		•
_	(ix)	FEATURE:
20		(A) NAME/KEY: misc_feature
		(B) LOCATION 1486
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:20:
25	ATGTTTT	TA AAACTTATCA AAAATTACTG GGCGCGAGCT GTTTGGCGCT GTATTTAGT
		GA ATGGTGGTGG CGGTGAATCG CCGGTTGAGA TGATTGCAAA TAGCGAGGG
	ACGTTTCA	AA TCGACTCCAA AGCAGATAGC ATTACTATTC AAGGCGTGAA GCTTAATAG
		TG CTGTCAATTT TGTTCCAGTA AGTGAGACGT TTCAAATGGG TGT <mark>TTTAA</mark> G
٠.		TC CAATCTCTAT ACAGGATTTT AAAGATATGG CAAGCACTTA TAAGATATT
0		GA AAGGGTTGGC AAACATAGCA AATAAAATTT CTCAATTAGA GCAAAAGGG
		GG AACCTCAAAC CCTTAATTTT GGAGAAAGTT TAAAAGGCAT TTCTCAAGG
	AAATAA	TA TAGAGGCAGA AATACAAACC GACAAAGGCG CTTGGACTTT TAACTTTGA
5	(2) INFO	RMATION FOR SEQ ID NO:21:
	(i)	SEQUENCE CHARACTERISTICS:
		(A) LENGTH: 1014 base pairs
		(B) TYPE: nucleic acid
0		(C) STRANDEDNESS: double
		(D) TOPOLOGY: circular
	(ii)	MOLECULE TYPE: DNA (genomic)
5	(iii)	HYPOTHETICAL: NO
	(iv)	ANTI-SENSE: NO
	(vi)	ORIGINAL SOURCE:
0 .	,	(A) ORGANISM: Helicobacter pylori
	(ix)	FEATURE:
	·/	(A) NAME/KEY: misc_feature
		(B) LOCATION 1 1014

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

		TAAAAGGTTT		TTAAAAACAA	GCTTATTAGC	TGGGGTTTTA	60
: _	CTAGGTGCTA	CICCICCII	AATGGCAAAG	CCTTTATTAA	GCGATGAAGA	CTTATTGAAA	120
5	CGAGTAAAAC	TACACAATAT	CAAAGAAGAT	ACGCTGACTA	GCTGTAATGC	TAAGGTGGAC	180
	GGCTCTCAAT	ACTTGAATAG	TGGTTGGAAT	TTATCTAAAG	AATTTCCGCA	AGAATATAGA	240
	GAAAAGATTT	TTGAATGCGT	AGAAGAAGAA	AAACATAAAC	AAGCCCTTAA	ጥጥጥልልጥሮአልጥ	300
	AAAGAAGACA	CTGAAGATAA	AGAAGAACTT	GCAAAAAAA	TCAAAGAAAT	TAAAGAAAAA	
	GCTAAAGTTT	TAAGGCAAAA	ATTTATGGCT	TTTGAAATGA	AAGAACACTC	TARAGAMAMA	360
10	CCAAATAAAA	AGCAACTTCA	AACCATGCTT	GAGAACCCTT	TTGATAATGG	AGGERANTE	420
	TTTATTGATG	ATTGGCACGA	ACCCTTTCCC	CCTATAACTA	GAGAGAATAC	AGCTGAAAGT	480
	CTTGGCATTA	AAGAATATAG	TGATGAAGGA	AAGATATTAG			540
	АТТАСАСААТ	ATAAAAAAAAA	TOTTOTAGGA	AAGATATTAG	CCTTTGGCGA	AAGAAGTTAT	600
•	GCTATGGCTA	ATATCACTCC	CCANAGGAA	AGCACTTATG	ATACTAGACA	AACCTTATCT	660
.15	CACCTCCATA	COMORNAMA	CGAAAACGAT	TATAAAATTA	CTTGGTTAAA	ACCCAAATAT	720
.13	ATAGAGCTAA	GIICAAATAA	TATTAAACCC	TTAATGTCAA	ACACAGAGTT	GTTAAATATG	780
	MINGAGCIAA	CCAATATCAA	AAAAGAATAT	GTTATGGGCT	GTAATATGGA	AATAGATGGT	840
-	TCTAAATATC	CCATTCATAA	AGATTGGGGA	TTTTTTGGTA	AGGCAAAAGT	CCCAGAAACT	900
	TGGAGAAATA	AGATTTGGGA	ATGTATTAAG	AATAAAGTAA	AGTCCTATGA	CAACACTACC	960
20	GCTGAAATAG	GAATAGTTTG.	GAAAAAAAT	ACTTATTCTA	TCTCTCATCA	CTAA	1014
20							
	(2) INFORMA	TION FOR SE	Q ID NO:22:				

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1251 base pairs
- (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: circular
- (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
- 35 (vi) ORIGINAL SOURCE:

25

- (A) ORGANISM: Helicobacter pylori
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
- 40 (B) LOCATION 1...1251
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

4.5	ATGAAAAAAT	TAGTTTTTAG	CATGCTTTTA	TGTTGTAAAA	GCGTGTTTGC	AGAGGGGGAA	60
45	ACTCCTTTGA	TTGTCAATGA	CCCAGAAACC	CATGTAAGTC	AAGCCACTAT	СУДОСССУУУ	120
	ATGGTAGATA	GTATCAAAAG	ATACGAAGAG	ATTATTTCTA	AGGCTCAAGC	ጥሮ እ አርጥሮ እ' አጥ	180
	CAGTTACAAA	AAGTCAATAA	CATGATAAAT	ACGACTAATT	ריידידים ביידים בי	ጥ አርጥ አርጥር ርጥ	240
	ATCACTTTAG	CCAATCCTAT	GCAAGTTTTA	CAAAACGCTC	AGTATCAAAT	እር እርእርርስምም	300
50	AGATACAACT	ATGAGAATTT	AAAGCAAAGC	ATAGAAAATT	GGAACGCACA	ע בהנהלולה עי עי ע	360
50	AGAAACAAAT	ACTTACAGCA	ACAATGCCCT	TGGCTTAATG	TCAATGCTCT	ምአረጥአ አረአ አ ም	420
	AAGATTGTCA	ATCTTAAAGA	TCTCAATAAC	CTAATCACCA	AAAATGGCGA	ACAAACCCAA	480
	ACCGCAAGAG	ATGTGCAAAA	TCTCATTCAG	TCCATTAGTG	GCAGTGGCTA	TOCANACATO	540
	CAATCACTTG	CTGGGGAATT	GAGTGGTAGA	GCGTGGGGGG	AAATGTTCTC	TAAAATCCTA	600
	AACGATAGTA	ATTATGAAAG	CGAGCAAGCT	CTTTTAGCAA	САСССААТАА	CCCAGAAGAC	660
55	CAAAAACGAA	GATTTTTGCT	TAGAGTAAAG	AAAAAGGTTA	ATGATAATAA	GCAGTTAAAA	720

5	GATAAACTTG ACCCATTTCT AAAAAGACTT GATGTCCTAC AAACTGAGTT TGGTGTAACT GACCCTACAG CTAACCATAA TAAGCAAGGG ATACATTATT GCACAGAAAA TAAAGAGACA GGTAAATGCG ACCCTATTAA AAATGTATTT AGGACAACTC GCTTAGATAA CGAATTAGAA CAAGAAATCC AAACGCTCAC ACTTGATTTA ATCAAAGCCT CCAATAAAGA CGCTCAAAGC CAAGCCTACG CAAATTTCAA TCAAAGGATT AAATTACTTA CTCTAAAATA TTTAAAAGAA ATTACCAATC AAATGCTCTT TTTAAATCAA ACAATGGCAA TGCAAAGCGA GATTATGACA GATGATTATT TTAGGCAAAA TAATGATGGC TTTGGGGAAA AAGAAAACCA TATAGACAAA CAATTAACGC AAAAAAGAAT AAACGAAAGA GAAAGAGCTA GAATATACTT TCAAAACCCT AATGTTAAAT TTGACCAATT TGGCTTTCCC ATTTTAGTA TATGGGATTA A	840 900 960 1020 1080
	(2) INFORMATION FOR SEQ ID NO:23:	
15	 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1131 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular 	
20	(ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO	
25	(iv) ANTI-SENSE: NO	•
25	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
30	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 11131 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:</pre>	
35	GTGAATAAGT GGATTAAAGG GGCGGTTGTT TTTGTAGGGG GTTTTGCAAC GATTACAACC TTTTCTTTAA TCTACCACCA AAAGCCAAAA GCCCCCCTAA ATAACCAGCC TAGCCTTTTG AATGACGATG AGGTGAAATA CCCCTTACAA GACTACACTT TCACTCAAAA CCCACAGCCA ACTAACACGG AAAGCTCCAA AGACGCTACC ATCAAAGCCT TACAAGAACA GCTCAAAGCC	60 120 180 240
40	GCTTTAAAAG CCCTAAACTC CAAAGAAATG AATTATTCCA AAGAAGAGC TTTTACTAGC CCTCCCATGG ATCCAAAAAC AACCCCCCCT AAAAAAGACT TTTCTCCAAA ACAATTAGAT TTACTGGCCT CTCGCATCAC CCCTTTCAAG CAAAGCCCTA AAAATTACGA AGAAAAACCTG ATTTCCCTG TGGATAACCC TAATGGCATT GATAGTTTCA CTAACCTTAA AGAAAAAGAC	300 360 420 480
• .	ATCGCCACTA ATGAAAACAA GCTTTTACGC ACCATTACAG CTGACAAAAT GATACCCGCT TTTTTGATTA CGCCCATTTC TAGCCAGATC GCTGGTAAAG TGATTGCGCA AGTGGAGAGC	540 600
<u>.</u> 45	GATATTTTTG CAAGCATGGG CAAAGCCGTC TTAATCCCCA AAGGCTCTAA AGTCATAGGC	660
7.7	TATTACAGCA ACAATAACAA AATGGGCGAA TACCGCTTGG ATATTGTATG GAGTCGAATC ATCACTCCCC ATGGCATTAA TATCATGCTC ACTAACGCTA AAGGGGCGGA CATTAAAGGC	720 780
	TATAACGGCT TAGTGGGGGA ATTGATTGAA AGGAATTTCC AACGCTATGG CGTGCCGTTA	840
	CTGCTTTCTA CGCTCACTAA CGGCCTATTG ATTGGGATCA CTTCGGCTTT AAACAACAGA	900
50	GGCAATAAAG AAGAGGTGAC TAATTTCTTT GGGGATTATC TTTTATTGCA ATTGATGAGG CAAAGCGGCA TGGGGATCAA TCAAGTGGTC AATCAAATTT TAAGAGACAA GAGCAAGATC	960
	GCCCCCATTG TGGTGATTAG AGAGGGGAGT AGGGTCTTCA TTTCGCCCAA TACTGACATC	1020
	TTCTTCCCTA TACCCAGAGA GAATGAAGTC ATCGCTGAGT TTTTGAAGTG A	1131
55	(2) INFORMATION FOR SEQ ID NO:24:	

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(i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 2751 base pairs
               (B) TYPE: nucleic acid
               (C) STRANDEDNESS: double
 5
              (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
        (iii) HYPOTHETICAL: NO
10
         (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
              (A) ORGANISM: Helicobacter pylori
15
         (ix) FEATURE:
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...2751
20
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:
     GTGGATTTGA GGATCCAATC TAAAGAAGTC AGTCATAATT TAAAGGAATT ATCAAAAACG
                                                                         60
     CTAATCAGCT ATCCTTTTGA AAAACATGTA GAAGCTTTAG GGGAACAATG CAGTAACTTC
                                                                        120
     GTTTCTATTC CCATTAACAA TGACGACTAT TCAAATATTT GCACTTTTGT GAGTGATTTT
                                                                        180
     ATAAATCTTA TAGCTTCTTA CAATTTATTA GAATCATTTT TAGATTTTTA TAAAGATAAA
     TTAAAATTGA GCGAGCTTGT AACTGAATAT GCCAACGTAA CCAATAATCT GCTTTTCAAA 300
     AAATTAATCA AACATTTAAG CGGCAACAAT CAATTGGTTA AAAATTTTTA TCAGTGTATA
     AGAGAAATTA TAAAATACAA CGCCCCTAAT AAAGAATACA AACCCAATCA ATTTTTTATA
                                                                        420
     ATAGGGAAAG GCAAACAAAA ACAATTAGCA AAAATTTATT CTCATTTAAA AGAACTTAGT
                                                                        480
30
    GCAAGTGAAA TTAAACCACA AGATATGGAA GACATCTTAA AAAAGCTAGA GGAATTAGAT
    AAAATTTTTA AAACTACCGA CTTTACAAAA TTCACACCAA AAACTGAAAT TAAGGATATT
                                                                        600
    ATTAAAGAAA TAGACGAAAA ATACCCTATC AATGAAAATT TTAAACGGCA ATTTAATGAG
                                                                        660
    TTTGAATCAA ATATTGAAAA ACATGATGAA ATAAAAAAGG ATTTTGAGCG AAACAAAGAG
                                                                        720
    TCGCTGATCC GAGAAATTGA AAATCACTGC AAAAATGAAT GCAATAGCGA AGAAGAGCCG
    GAGTATAAGA TTAATGATCT GCTCAAAAAT ATCCAACAAA TATGCAAAAA TTATATAGAA
                                                                        840
    AGTCATGCCG TTAATGATGT GTCTAAAGAT ATTAAATCCA TGATGTGTCA GTTTTATTTG
                                                                        900
    AAACAGATAG ATTTATTAGT CAATTCAGAA ATTGTGCGAT ACAGATACAG CAATCTTTTT
    GAACCAATAC AAAGATCTTT ATGGGAGAGT ATAAAAATTT TAGATAATGA AAGTGGCATT
    TATTTGTTCC CTAAAAATAT TGGTGAAATC AAGGATAAAT TTGAAGCAAA CAAGGAAAAA
    TTCAAACAAA GCAAAAATGT TTCTGAGTTC GCAGAATATT GCCGAGAGTG TAACCCCTAT
    ACAGCGTTTA ACTTTCATCT AAATATAAAT AATGGTTTAT CTCATCAATT TGAAAAATTC
    GTGCCAATCA TGAAAGAATA CAAAGAGCCA AAAATCACAG ATAATGACCT TGAAGCCATA
    TCAACCAAAG AGACTGGTCT TGCTAGCCAA TTATCTGGGC ACTGGTTTTT TCAGCTTTCG 1320
    TTATTTAATA AAACAAACTT TAATCCTAAT AAAATTTGGA TTCCTTTAGA GTTCAATAAA 1380
    AGATCAAAAA TAAAGTTTGA TAAAGATTTA GAAATCTATT TTGATAGTCA TGAATCGTTC 1440
    AATATCTCTA AAAAATACTT GCAAGAAATA GATCAAGAAT CACTAAAAAA GATCAAACAA 1500
    TCAAAAGATT TTTTTCAAT TCAAAAAATA GAGAGTAAGC ATGATAATAA CGATATACTG 1560
    CAACTTGAAT TTTTTGAGAA TGATACAAGT TTTCTTTTTG CTAAAGGAAG TTTTGCAGAA 1620
    ATTTTAGAAT ACAACATGCA ATTAAAAATA GATTCTTTAA TTACAAAAGA ATTTAATAAG 1680
    CTTTTAGCGA TCGTTCAAGA TAGTCCCCAA GATAGTTACC AATTAAAAAT TCGTGTCCGA 1740
    CATAACAATA AGCTTCCTAG AGAGAAATAT ACGGAACATG AAATAAAACT TGAAGTTTAT 1800
    GATTGCAGAA AATCCCACGA TCACAATGAG CCAATCATCT TAAGCCAGCA AAGCACCGGC
    TTCCAATGGG CGTTTAATTT CATGTTTGGC TTTCTTTATA ATGTGGGATC ACATTTTAGT
    TTTAACCATA ATATTATCTA TGTCATGGAC GAGCCAGCCA CTCATTTGAG CGTGCCAGCC
    AGAAAGGAGT TTAGGAAATT TTTAAAAGAA TACGCTCATA AAAATCATGT TACTTTTGTT
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	TTAGCCACCC ATGACCCCTT TTTAGTGGAT ACGGATCATT TAGATGAAAT AAGGATTGTG	2100
	GAAAAGGAAA CAGAAGGCTC TGTAATTAAG AATCACTTTA ACTATCCCCT AAATAATGCA	2160
	AGCAAAGACT CCGACGCTTT GGACAAAATC AAACGCTCTT TAGGAGTGGG CCAGCATGTT	2220
	TTTCATAACC CCCAAAAACA CCGAATCATT TTTGTAGAAG GCATCACGGA TTATTGTTAT	2280
5	TTGAGCGCTT TTAAATTGTA TTTGCGTTAC AAAGAATACA AGGACAACCC CATTCCTTTC	2340
• .	ACTITCTTAC CCATTICAGG GCTTAAAAAC GATTCAAACG ATATGAAAGA AACCATTGAA	2400
	AAACTTTGCG AGTTAGACAA TCACCCTATT GTTTTGACAG ACGATGACAG AAAATGCGTT	2460
•	TTTAACCAAC AAGCAACGAG CGAACGATTT AAAAGAGCTA ATGAAGAAAT GCATGATCCC	2520
	ATCACCATCC TACAACTCTC AGACTGCGAT AGGCATTTCA AACAAATTGA AGATTGTTTC	2580
10	AGCGCAAACG ATAGAAACAA ATACGCTAAA AATAAGCAAA TGGAATTGAG CATGGCTTTT	
	AAAACAAGGC TTTTGTATGG CGGAGAAGAT GCGATAGAAA AACAAACAAA AAGAAATTTT	2700
	TTAAAATTAT TCAAATGGAT TGCATGGGCT ACAAACTTGA TCAAAAACTA A	2751
1.5	(2) INFORMATION FOR SEQ ID NO:25:	
15	() CROSSINGE GUADA CHIED YORK CO	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 531 base pairs (B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
20	(D) TOPOLOGY: circular	
20	(b) Toronogi. Circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
25		
	(iv) ANTI-SENSE: NO	•
	(vi) ORIGINAL SOURCE:	
20	(A) ORGANISM: Helicobacter pylori	
30		
	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature</pre>	
	(B) LOCATION 1531	
	(B) LOCATION 1331	
35	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:	
	ATGACTGCAA TGATGCGTTA TTTTCACATC TATGCGACCA CTTTTTCTT CCCTTTGGCG	60
	CTTCTTTTTG CGGTTAGTGG GCTTTCATTG CTCTTTAAAG CGCGCCAAGA CACTGGCGCT	120
	AAGATCAAAG AATGGGTTTT AGAAAAATCC TTAAAAAAAG AAGAACGATT GGACTTTTTA	180
40	AAAGGCTTTA TAAAAGAAAA CCATATCGCT ATGCCTAAAA AGATAGAGCC TAGAGAGTAT	240
	AGGGGAGCGT TAGTCATTGG CACGCCTTTG TATGAAATCA ACCTTGAAAC TAAAGGCACT	300
	CAAACGAAAA TCAAGACCAT TGAAAGGGGC TTTTTAGGCG CGCTCATCAT GCTGCATAAG	360
•	GCTAAGGTGG GCATCGTGTT TCAGGCGCTT TTAGGGATTT TTTGCGTGTT TTTATTGTTG	420
15	TTTTACTTGA GCGCGTTTTT AATGGTGGCT TTTAAAGACA CTAAACGCAT GTTTATAAGC	480
45	GTTTTAATAG GGAGCGTGGT GTTCTTTGGA GCGATCTATT GGTCTTTGTA G	531
	(2) INFORMATION FOR SEQ ID NO:26:	
	(2) INFORMATION FOR BEY ID NO:20:	
	(i) SEQUENCE CHARACTERISTICS:	
50	(A) LENGTH: 669 base pairs	
	(B) TYPE: nucleic acid	•
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
,		
55	(ii) MOLECULE TYPE: DNA (genomic)	

	() III OIMII CAL. NO	
5	(iv) ANTI-SENSE: NO	
٠	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
10	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1669</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:	
15	ATGTTTAAAA ACGCTTTAAA TATACAAGAT TTTTCATTTA AAAATCATAC TAGTACAGCC ATTATTGGCA CAAATGGTGC TGGAAAATCA ACGCTTATCA ACACTATTCT AGGCATTAGA	60 120
20	TCAGACTATA ATTTTAAAGC ACAAAACAAT AATATTCCAT ACCACGACAA TGTTATACCA CAACGCAAGC AATTGGGAGT TGTCTCTAAC CTATTCAACT ACCCACCTGG ATTAAACGCA AACGACCTTT TTAAATTCTA TCAATTTTTT CACAAAAACT GCACTCTAGA TTTGTTTGAA AAAAATCTTT TAAATAAAAC CTACGAACAC CTAAGCGACG GACAAAAACA GCGCTTAAAA	180 240 300
	TIGACTIAG CICTIAGCCA TCACCCACAA TTAGTTATTA TGGATGAACC AGAAACCAGT TTAGAGCAAA ACGCTCTTAT AAGACTATCA AATCTCATAA GCTTGCGCAA CACCCAACAA CTTACAAGTA TCATCGCCAC TCATGATCCT ATTGTCTTAG ATAGTTGCGA ATGCCTATTC	420 480 540
25	CTCCTTAAGA ATGGCAACAT TGCTCAATAC AAACCTTTAA ATTCTATATT AAAATCTGTA GCTAAAACTT TTAACTTTAA AGAAAAACCA ACCACAAAAG ACTTATTAGC GTTACTAAAG GATATTTAA	600 660 669
	(2) INFORMATION FOR SEQ ID NO:27:	
30	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1221 base pairs (B) TYPE: nucleic acid	
35	(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
	(iii) MOLECULE TYPE: DNA (genomic)	
40	(iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO	
•	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
45	(ix) FEATURE: (A) NAME/KEY: misc feature	
	(B) LOCATION 11221	
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:	
	ATGTATGCGG CTCATCCTAT TAAACCCATA AAAGCCCCTA AACTCAAATC TCAATTTTTA AGGCGTGTGT TTGTGGGCGC GTCCATTAGG CGCTGGAATG ACCAAGCATG CCCTTTGGAA TTTGTGGAAT TAGACAAGCA AGCCCATAAA GCGATGATTG CGTATCTGCT CGCTAAAGAT	60 120 180
55	TTAAAAGATA GGGGTAAAGA TTTAGATTTA GATCTTTTAA TCAAATATTT TTGCTTTGAG TTTTTTGGAGC GCTTGGTTTT AACCGATATT AAACCCCCTA TTTTTTACGC CCTCCAACAA	240 300

900

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	ACGCATAGTA AAGAGTTAGC TTCCTATGTT GCGCAAAGTT TGCAAGATGA AATCAGTGCG	360
	TATTTTTCTT TAGAGGAACT CAAAGAGTAT TTAAGCCACA GGCCTCAAAT TTTAGAAACT	420
	CAAATTTTAG AGAGCGCGCA TTTTTATGCG TCTAAGTGGG AGTTTGATAT TATCTATCAT	480
٠.٠	TTTAACCCCA ACATGTATGG CGTGAAAGAG ATTAAAGATA AAATTGACAA GCAACTCCAC	· 540
5	AATAACGATC ATTTGTTTGA AGGGCTTTTT GGGGAAAAAG AAGATTTGAA AAAATTGGTG	600
	AGCATGTTTG GGCAGTTGCG TTTCCAAAAG CGCTGGAGCC AAACCCCAAG AGTGCCACAA	660
	ACCAGTGTTC TAGGGCATAC TTTATGCGTG GCGATTATGG GGTATTTATT GAGTTTTGAC	720
	TTGAAAGCTT GTAAAAGCAT GCGGATCAAT CATTTTTTGG GCGGGCTTTT CCATGATTTA	780
10	CCCGAAATTT TAACCCGAGA CATTATCACG CCCATCAAAC AAAGCGTTGC AGGGCTTGAT	840
10	CATTGCATTA AAGAGATTGA AAAAAAGGAA ATGCAAAACA AAGTCTATTC CTTTGTGTCT	900
	TTGGGCGTTC AAGAAGATTT GAAATATTTC ACCGAAAACG AGTTTAAAAA CCGCTACAAA	960
	GACAAGTCTC ATCAAATCGT TTTCACTAAA GACGCTGAAG AATTATTCAC GCTTTATAAT	1020
	AGCGATGAAT ATCTTGGGGT TTGCGGGGAG CTTTTGAAGG TGTGCGATCA TTTGAGCGCG	1080
1.5	TTTTTAGAAG CCCAAATCTC TCTTTCTCAT GGCATTTCTA GCTACGATTT AATCCAAGGA	1140
15	TIGHTINGA TITAGGAAA	1200
	TTGTTTAGAG ATTTTAAGTA A	1221
	(2) INFORMATION FOR SEQ ID NO:28:	
20		
20	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1008 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
25	(D) TOPOLOGY: circular	
25	(3.1) NOT DOTT B. INVDE. DAYS. (many 1.1)	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
·		
30	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
		•
35	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
	(B) LOCATION 11008	
•		
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:	
40		
	GTGTTGTGGG TGCTATATTT TTTAACCAGT TTATTTATTT GCTCTTTGAT TGTTTTGTGG	60
	TCTAAAAAAT CCATGCTCTT TGTGGATAAC GCTAATAAAA TCCAAGGCTT CCATCATGCA	120
:	AGAACCCCAC GAGCCGGGGG GCTTGGGATC TTTCTTTCTT TTGCGTTGGC TTGTTATCTT	180
4.5	GAACCTTTTG AGATGCCTTT TAAGGGGCCT TTTGTTTTCT TAGGGCTATC GCTAGTGTTT	240
45	TTGAGCGGTT TTTTAGAAGA CATTAACCTT TCATTAAGCC CCAAAATACG CCTTATTTTG	300
	CAAGCTGTAG GGGTCGTTTG CATCATTTCA TCAACGCCTT TAGTGGTGAG CGATTTTTCG	360
	CCCCTTTTTA GCTTGCCTTA TTTCATCGCT TTTTTATTCG CTATTTTTAT GCTGGTGGGT	420
	ATCAGTAACG CTATTAATAT CATTGACGGG TTTAACGGGC TTGCATCTGG GATTTGCGCG	480
50	ATCGCGCTTT TAGTCATTCA TTATATAGAC CCTAGCAGTT TGTCTTGTTT GCTCGCTTAC	540
50	ATGGTGCTTG GGTTTATGGT GTTAAATTTC CCTTCAGGAA AGATTTTTTT AGGCGATGGG	600
	GGGGCGTATT TTTTGGGTTT GGTGTGCGGG ATTTCTCTCT TGCATTTGAG TTTGGAGCAA	660
	AAAATCAGCG TGTTTTTTGG GCTCAATTTA ATGCTTTATC CGGTCATAGA GGTGCTTTTT	720
	AGTATCCTTA GGCGCAAAAT AAAACGCCAG AAAGCCACCA TGCCGGATAA TTTGCATTTG	780
	CACACCCTTT TATTTAAATT CTTGCAACAA CGCTCTTTCA ATTACCCTAA CCCTTTATGC	840
55	GCGTTTATCC TTATTCTATG CAACCTGCCT TTTATTTTAA TAACCGTTTT GTTTCGCTTC	000

GCGTTTATCC TTATTCTATG CAACCTGCCT TTTATTTTAA TAAGCGTTTT GTTTCGCTTG

	GACGCTTATG CGCTCATTGT GATTAGCCTA GTCTTTATCG CATGCTATTT AATAGGCTAT GCTTATTTGA ATAGGCAAGT TTGCGCTTTA GAAAAGCGGG CGTTTTAA	960 1008
5	(2) INFORMATION FOR SEQ ID NO:29:	
10	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 291 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
15	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
20	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1291</pre>	
25	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:	
30	ATGGCTTTTA AAAGCGGTGC CAACAAGAAT CCTGTCATGA CCGCGCAAGC TAAAAAATTA AGCGATGAAG ACATCAAAGC TTTAGCCAAA TACATGGGGA CTGTCAAAA	60 120 180 240 291
	(2) INFORMATION FOR SEQ ID NO:30:	
35	(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 471 base pairs(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
40	(ii) MOLECULE TYPE: DNA (genomic)	
:	(iii) HYPOTHETICAL: NO	
45	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
50	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1471</pre>	
55	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:	

5	GAAAAACT GGGAAAAG TCAAACAT AGAGAAGA TTTTTAAA AAACGCTT	TT TCAATAACAT TGG ATCTGAGTT TGG TCCTTATTGC GG AAGTGAACT GG AACAAGCCT ATCTGACAGACAG ATCTGACAGACAGACAG ATCTGACAGACAGACAG ATCTGACAGACAGACAGACAG ATCTGACAGACAGACAG ATCTGACAGACAGACAGACAGACAGACAGACAGACAGACA	TAAAGATGC SAGCCTTTTA SATCGCGCCT TTTAGTTATT ATCTAAAAAC ATTCAGCCAG	TTGAGCGCGA GGGGCGTTTG TTTTTAGACA AGCGTGATTA ACGCTCAAAG AATGAACTCA	TTAGTGGGGC GGCTTAAAGA CGGAAGAATA AAAAAGAAAA CGTTATTAAA ACGATATTTT	TAGTGGGGTG GAGCAACGCT CGGCATTTTT AACACGCTAT GGGGCTTATT AATGCTCTCC	60 120 180 240 300 360 420 471
10	(2) INFO	RMATION FOR SEC) ID NO:31:	:			
15	(i)	SEQUENCE CHARA (A) LENGTH: 3 (B) TYPE: nuc (C) STRANDEDN (D) TOPOLOGY:	57 base pa leic acid MESS: doubl	airs			
	(ii)	MOLECULE TYPE:	DNA (geno	omic)			
20	(iii)	HYPOTHETICAL:	NO				
	(iv)	ANTI-SENSE: NO	·		•	·	
25		ORIGINAL SOURC		ter pylori			
30	,	FEATURE: (A) NAME/KEY: (B) LOCATION SEQUENCE DESCR	1357				
35	GTGATGCTZ ATGAGTTTZ TTAAATGA AGCAGAAAC AAAGAACAZ	AA TGGCAATTT TAT TCGCCAATAT GOT TTGTTTTTGG TGG CTATGGAAAA TGG TAGATATTAG AG ATTTTGTTAT T	ACCCCTTAT GGGTTGGAG ATAGAAGTG CATCTTATC GAATTTGAG	ATTCTTATTT CAAATTTTTT GGGCTTGATA GGTCTTTTTG GATTTACGCC	TGAAAATGAT GCAACAGAGA GCAATGCGAG TCCAAGCTCA AGGCTTTTGG	CATTAAAGAT AAAAAATCGT ATTAAATTTT AAATGATACT	60 120 180 240 300 357
40	(2) INFO	MATION FOR SEQ	ID NO:32:				
45	(i)	SEQUENCE CHARA (A) LENGTH: 1 (B) TYPE: nuc (C) STRANDEDN (D) TOPOLOGY:	068 base p leic acid ESS: doubl	pairs			
	(ii)	MOLECULE TYPE:	DNA (geno	mic)			
50	(iii)	HYPOTHETICAL:	NO			•	
	(iv)	ANTI-SENSE: NO					
	(vi)	ORIGINAL SOURC	E:				

(A) ORGANISM: Helicobacter pylori

240

300

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(ix) FEATURE:
               (A) NAME/KEY: misc_feature
                (B) LOCATION 1...1068
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:
      ATGAATATCA AAATTTTAAA AATATTAGTT GGAGGGTTAT TTTTTTTGAG CTTGAACGCC
      CATTTATGGG GGAAACAAGA CAATAGCTTT TTAGGGATTG GTGAAAGAGC CTATAAAAGC
                                                                          120
      GGGAATTATT CTAAAGCGGC GTCTTATTTT AAAAAAGCAT GCAACGATGG GGTGAGTGAA
 10
                                                                          180
      GGCTGCACGC AATTAGGAAT CATTTATGAA AACGGGCAAG GCACTAGAAT AGATTATAAA
                                                                          240
     AAAGCCCTAG AATATTATAA AACCGCATGC CAGGCTGATG ATAGGGAAGG GTGTTTTGGC
                                                                          300
      TTAGGGGGGC TTTATGATGA GGGTTTAGGC ACGGCTCAAA ATTATCAAGA AGCCATTGAC
                                                                          360
     GCTTACGCTA AGGCATGCGT TTTAAAACAC CCTGAGAGTT GCTACAATTT AGGCATCATT
                                                                          420
     TATGATAGAA AAATCAAAGG CAATGCCGCT CAAGCGGTTA CTTACTATCA AAAAAGCTGT
15
                                                                          480
     AATTTTGATA TGGCTAAGGG GTGTTATATT TTAGGCACTG CCTATGAAAA AGGCTTTTTA
                                                                          540
      GAAGTCAAAC AGAGCAACCA TAAAGCCGTT ATCTATTATT TGAAAGCGTG CCGATTGAAT
     GAGGGCAGG CTTGCCGAGC GTTAGGGAGT TTGTTTGAAA ATGGCGATGC AGGGCTTGAT
     GAAGATTTTG AAGTGGCGTT TGATTATTTG CAAAAAGCTT GCGCTTTAAA CAATTCTGGT
     GGTTGCGCGA GTTTAGGCTC TATGTATATG TTGGGCAGGT ATGTTAAAAA AGACCCCCAA
20
     AAGGCTTTTA ACTATTTCAA GCAAGCATGC GATATGGGGA GCGCGGTGAG TTGCTCTAGG
                                                                          840
     ATGGGCTTTA TGTATTCGCA AGGGGACACT GTTTCAAAAG ACTTGAGGAA AGCCCTTGAT
                                                                          900
     AATTATGAAA GAGGTTGCGA TATGGGCGAT GAAGTGGGTT GCTTCGCTCT AGCGGGCATG
                                                                          960
     TATTACAACA TGAAAGATAA AGAAAACGCC ATAATGATTT ATGACAAGGG CTGTAAATTG
                                                                        1020
25
     GGCATGAAAC AGGCATGCGA AAATCTCACC AAACTCAGGG GGTATTAG
                                                                         1068
     (2) INFORMATION FOR SEQ ID NO:33:
         (i) SEQUENCE CHARACTERISTICS:
30
               (A) LENGTH: 582 base pairs
               (B) TYPE: nucleic acid
               (C) STRANDEDNESS: double
               (D) TOPOLOGY: circular
35
         (ii) MOLECULE TYPE: DNA (genomic)
        (iii) HYPOTHETICAL: NO
         (iv) ANTI-SENSE: NO
40
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
45
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...582
       (xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:
    ATGAAAGAAA AAAACTTTTG GCCTTTAGGA ATCATGAGCG TGCTTATTTT TGGGCTTGGG
50
                                                                          60
    ATCGTGGTGT TTTTAGTGGT GTTTGCCCTA AAAAATTCGC CTAAAAATGA TTTAGTGTAT
                                                                         120
    TTCAAGGGTC ATAACGAAGT GGATTTAAAC TTTAACGCCA TGCTTAAAAC TTATGAAAAC
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TTTAAATCCA ATTATCGTTT TTCAGTGGGT TTAAAGCCTC TTACCGAAAG CCCTAAAACC

CCCATTTTGC CCTATTTTC TAAAGGCACG CATGGGGATA AAAAAATCCA AGAAAACCTT

TTAAACAACG CTTTGATTTT AGAAAAGTCC AACACGCTTT ATGCACAATT GCAACCGCTC

(iii) HYPOTHETICAL: NO

AAACCCGCTT TAGATTCGCC AAATATTCAA GTGTATTTAG CGTTCTATCC CAGCCAATCC CAGCCCAGAT TATTAGGAAC GCTTGATTGT AAAAACGCAT GCGAACCTTT AAAATTTGAT 480 TTGTTAGAGG GCGATAAAGT GGGGCGCTAT AAGATCCTTT TTAAATTTGT TTTTAAAAAT 540 AAAGAAGAAT TGATTTTGGA GCAACTGGCT TTTTTTAAGT AG 582 (2) INFORMATION FOR SEQ ID NO:34: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 870 base pairs 10 (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular (ii) MOLECULE TYPE: DNA (genomic) 15 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 20 (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc_feature 25 (B) LOCATION 1...870 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:34: TTGGGTATCA ATATGTGTTC TAAAAAAATA AGAAATCTCA TTTTATGCTT TGGTTTTATT 60 30 TTAAGCTTGT GCGCTGAAGA AAATATCACC AAAGAAAACA TGACTGAAAC GAACACGACT GAAGAAAACA CCCCTAAAGA CGCTCCCATT CTTTTGGAAG AAAAACGCGC CCAAACTCTA GAGCTTAAAG AAGAAAATGA AGTGGCAAAA AAGATTGATG AAAAAAGCCT GCTTGAAGAA ATCCATAAGA AAAAACGCCA GCTTTACATG CTCAAAGGGG AATTGCATGA AAAGAATGAA TCCATCTTAT TCCAACAAAT GGCTAAAAAT AAGAGCGGCT TTTTTATAGG CGTGATCCTT GGCGATATAG GGATTAACGC TAATCCTTAT GAGAAGTTTG AACTTTTAAG CAATATTCAA GCTTCTCCCT TGCTGTATGG TTTAAGGAGC GGGTATCAAA AGTATTTCGC TAACGGGATT AGCGCCTTAC GCTTTTATGG GGAATATTTA GGGGGGGCGA TGAAAGGGTT TAAAAGCGAT TCTTTAGCTT CTTATCAAAC CGCAAGCTTG AATATTGATC TGTTGATGGA TAAGCCTATT 600 GACAAAGAAA AAAGGTTTGC GTTAGGGATA TTTGGAGGCG TTGGAGTGGG GTGGAATGGG ATGTATCAAA ATTTAAAAGA GATTAGAGGG TATTCACAGC CTAACGCCTT TGGGTTGGTG TTAAATTTAG GGGTGAGCAT GACGCTCAAC CTCAAACACC GCTTTGAATT AGCCCTAAAA ATGCCTCCCT TAAAAGAAAC TTCGCAAACC TTTTTATATT ATTTTAAAAG CACTAATATT TATTATATTA GTTACAACTA TTTATTGTAA 870 45 (2) INFORMATION FOR SEQ ID NO:35: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 2007 base pairs (B) TYPE: nucleic acid 50 (C) STRANDEDNESS: double (D) TOPOLOGY: circular (ii) MOLECULE TYPE: DNA (genomic)

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(iv) ANTI-SENSE: NO
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(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

(ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION 1...2007

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

	GGCTTTTTCA	TAGAAGCCGG	CTTTGAAACT	GGGCTATTAG	AAGGCACACA	AACGCAAGAA	120
15	AAAAGACACA	CCACCACAAA	AAACACTTAC	GCAACTTACA	ATTATTTACC	CACAGACACG	180
-	ATTTTAAAAA	GAGCGGCTAA	TTTATTCACC	AATGCCGAAG	CGATTTCAAA	יישייי איני איני איני איני איני איני	240
	TCATCTTTAT	CCCCTGTTAG	AGTGTTGTAT	ATGTATAATG	GTCAATTAAC	TATAGAAAAC	300
	TTCTTGCCTT	ATAATTTAAA	TAATGTTAAG	CTTAGTTTTA	CAGACGCTCA	AGGCAACACG	360
••	ATTGATCTAG	GCGTGATAGA	GACCATCCCC	AAACACTCTA	AGATTGTTTT	ACCCGGGGAG	420
20	GCGTTTGATA	GTTTAAAAGA	GGCGTTTGAT	AAAATTGACC	CCTATACTTT	Σ ליין לאינו אין	480
	AAATTTGAAG	CCACTAGCAC	TTCTATTTCT	GATACTAACA	CGCAGAGGGT	GTTTGAAACG	540
	CTCAATAACA	TTAAAACAAA	TCTTATAATG	AAATATAGTA	ATGAAAATCC	ΑΑΔΟΔΔΤΤΤΟ	600
	AACACTTGTC	CTTACAATAA	TAATGGTAAT	ACAAAAAATG	ATTGTTGGCA	AAATTTCACC	660
	CCACAAACCG	CAGAAGAATT	CACCAATTTA	ATGTTGAACA	TGATCGCTGT	CTTACACTCC	720
25	CAATCTTGGG	GCGATGCGAT	CTTAAACGCT	CCTTTTGAAT	TCACTAACAG	СТСДДСДСДТ	780
	TGCGATAGCG	ATCCTTCAAA	ATGCGTAAAT	CCCGGAGTAA	ATGGGCGTGT	ТСАТАСТАВА	840
	GTCGATCAAC	AATATATACT	CAACAAACAA	GGTATTATTA	ATAATTTTAG	ΔΔΔΔΔΔΔΤΛ	900
	GAAATTGATG	CGGTTGTTTT	AAAAAATTCA	GGGGTTGTAG	GGTTAGCCAA	TEGATATECC	960
20	AATGATGGTG	AATATGGCAC	ATTAGGGGTA	GAAGCCTATG	CTTTAGATCC	Таааааастс	1020
30	TTTGGCAACG	ACCTTAAGAC	TATCAATTTA	GAAGATTTAA	GAACCATCTT	GCATGAATTC	1080
	AGCCACACTA	AAGGCTATGG	GCATAACGGG	AATATGACCT	ATCAAAGAGT	GCCGGTAACG	1140
	AAAGATGGTC	AAGTGGAAAA	GGATAGTAAT	GGCAAGCCAA	AAGATTCTGA	TGGCCTCCCC	1200
	TATAATGTGT	GTTCGCTTTA	TGGGGGATCC	AATCAGCCCG	CTTTCCCTAG	CAACTACCCT	1260
25	AATTCCATCT	ATCACAATTG	TGCGGATGTC	CCGGCTGGCT	TTTTAGGGGT	AACAGCAGCG	1320
35	GTTTGGCAGC	AGCTCATCAA	TCAAAACGCC	TTGCCGATCA	ACTACGCTAA	СТТССССАСТ	1380
	CAAACAAACT	ACAACCTAAA	CGCTAGTTTA	AACACGCAAG	ATTTAGCCAA	ጥጥርር እጥርር ርጥር	1440
	AGCACCATCC	AAAAAACCTT	TGTAACTTCT	AGCGTTACCA	ACCACCATTT	ምምሮል አልሮሮሮ ል	1500
	TCGCAAAGTT	TTAGAAGCCC	TATTTTAGGG	GTTAACGCTA	AAATAGGCTA	TCAAAACTAC	1560
40	TITAATGATT	TCATAGGGTT	GGCTTATTAT	GGCATCATCA	AATACAATTA	СССТАААССТ	1620
40	GTTAATCAAA	AAGTCCAGCA	ATTGAGCTAT	GGTGGGGGGA	TAGATTTGTT	ልጥጥርር:ልጥጥጥ ር	1680
	ATCACCACTT	ACTCCAATAA	AAATAGCCCT	ACAGGCATTC	AAACCAAAAG	CD ջարարարարար	1740
-	TCATCTTTTG	GTATCTTTGG	GGGGTTAAGG	GGCTTGTATA	ACAGCTATTA	ТСТСТТСААС	1800
	AAAGTCAAAG	GAAGCGGCAA	TTTAGATGTG	GCTACCGGGT	TGAACTACCG	СТАТААССАТ	1860
Ä5	TCTAAATATT	CTGTAGGGAT	TAGCATCCCT	TTAATCCAAA	GAAAAGCTAG	CCTCCTTTTCT	1920
45	AGCGGTGGCG	ATTATACGAA	CTCTTTTGTT	TTCAATGAAG	GGGCTAGCCA	CTTTAAGGTG	1980
	TTTTTCAATT	ACGGGTGGGT	GTTTTAG				2007
•							

ATGAGAAAAC TATTCATCCC ACTTTTATTA TTCAGCGCTT TAGAAGCGAA CGAGAAAAAC

(2) INFORMATION FOR SEQ ID NO:36:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 192 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: circular

- 115 -

	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
5	(iv) ANTI-SENSE: NO	
٠	<pre>(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori</pre>	
10	(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1192	
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:	
20	ATGAATACAG AAATTTTAAC CATCATGTTA GTTGTCTCCG TGCTTATGGG ATTGGTAGGC TTAATAGCGT TTTTATGGGG GGTTAAAAGC GGTCAGTTTG ACGATGAAAA ACGCATGCTT GAAAGCGTGT TGTATGACAG CGCGAGCGAC TTGAACGAAG CGATTTTACA AGAAAAACGC CAAAAGAATT AA	60 120 180 192
20	(2) INFORMATION FOR SEQ ID NO:37:	
25	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1221 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular	
30	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
35	<pre>(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori</pre>	•
1 0	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 11221</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:	
15	ATGGTATTT TTCATAAGAA AATTATTTA AATTTTATCT ATTCTTTAAT GGTTGCTTTT TTATTCCATT TATCCTATGG GGTTCTTTTA AAAGCCGATG GAATGGCTAA AAAGCAAACT CTTTTAGTGG GTGAAAGGCT TGTGTGGGAT AAGCTCACGC TGTTAGGGTT TTTAGAAAAA	60 120 180
:	AACCATATCC CCCAAAAACT CTACTACAAT TTGAGCTCTC AAGATAAAGA ATTGAGTGCT GAAATCCAAA GCAATGTTAC CTACTACACT TTAAGAGATG CAAATAACAC GCTCATTCAA GCCCTTATCC CTATTAGCCA GGATTTGCAA ATCCATATTT ACAAAAAAGG AGAGGATTAT	240 300
50	TTTTTAGACT TTATCCCCAT TGTTTTCACT CGTAAAGAAA GAACCCTCCT TCTTTCCTTA CAAACTTCGC CCTATCAAGA TATTGTCAAA GCCACCAATG ACCCCCTTTT AGCCAACCAA TTGATGAACG CGTATAAAAA AAGCGTGCCT TTTAAACGCC TAGTGAAAAA CGATAAAATC	360 420 480 540
55	GCTATCGTTT ATACAAGGGA TTATCGTGTG GGGCAAGCGT TTGGCCAGCC GACCATCAAA ATGGCGATGG TTAGCTCTCG TTTGCACCAA TACTATCTTT TTTCCCATTC AAACGGGCGT TATTACGATT CAAAAGCGCA AGAAGTGGCA GGGTTTTTAC TAGAAACCCC GGTGAAATAC	600 660 720

5	ACCCGCATTT CTTCGCCTTT TTCGTATGG AGGTTCCATC CTGTTTAAA AGTTAAACGG CCTCATTACG GCGTGGATTA TGCGGCTAAA CATGGCAGTT TGATCCATTC TGCTTCAGAC GGCCGTGTGG GTTTTATAGG GGTTAAGGCG GGTTATGGGA AGGTGGTTGA AAAAAAGGCC AATCATAGGA AGAGTGGGAA GCACGGGTTT AAAAAAAAGGC CCGCATTTGC ATTTTGGCGT GTATAAAAAC TCCCGCCCCA TTAATCCTTT AGGCTATATC CGCACCGCTA AAAAAATTAGA AGAACTTTTT AAAACCCATT CTTTTGAAAA AAATTCATTT TATCTTTTAG AGGGTTTTTA A	840 900 960 1020
	(2) INFORMATION FOR SEQ ID NO:38:	
15	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 891 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular	
20	(ii) MOLECULE TYPE: DNA (genomic)	
20	(iii) HYPOTHETICAL: NO	
	(111) INFOIRETICAL: NO	
	(iv) ANTI-SENSE: NO	
25	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature</pre>	
30	(B) LOCATION 1891	٠
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:	
<u>.</u> _	TTGTTTTTAG TCAAAAAAT AGGCGTGGTA ATAATGATTT TAGTCTGCTT TTTAGCTTGC	_
35	TOCKHOAGA GCITTATCAA AATGCAAAAA AAAGCCCAAC ACGAAGAAAA	60 120
	THE COCCOCA GCIAIGIGGA TICGGATTAT CANCEUTIPE COCARAGON TO THE	180
	THE PROPERTY AND A CONTRACT OF THE PROPERTY OF	240
	GACAATTCTT TTAACCCTGA AAATTCCGTG ATTTTACTGA ATGAGCCAAG CGATAATAGT GAAAAAAACC TACTCTCATA CCCAAACGAT CCCAATAACA ATGAAGACAA CGCTAATAAT	300
40	TOTOMORM MICCUITCT TTACAAGEEE ANNANANA CARARAGEE	360
	CIMITALICCE MACAMBATTI CTACCCCCTA AAAAATCCCC AMAMMA MOAM AAAAAAAAAAAAAAAAAAAAAAA	420
•	SELL COLLOSINON RAILLANITT ADACCOMPANY ACCOMPANY ACCOMPANY	480 540
•	TOUR TENED A LOCK AGAI CCAAA("I"I"I" ACTOMONINO NO NOT CONTRACTOR	600
45	CAAATTAAGG GCAAAATTTC TTCGTATGTT TATACCACCA ATAACGGTAG CTTGAGTTTA AGGCCTTTTT ATGAATCGTT TTTGTTAGAA AAAAAGAGCG ATAATGTTTA TACGATAGAG AATAAGGCTT TAGATAGTAT GCAATAGAG	660
	THE TACKLACIAL GCAGATTTCA AACTCTCAAA MCCMCMMAAA	720
	THURCAGULA GUATAAAGUU ATCAGTATTU ATTTUOCATUM TAAAAAGU	780
	CGCTTTAAGA GCGATACGGA ACTCTTTTTA GAATGTCTTA AGGAAAGTTA G	840 891
50	(2) INFORMATION FOR SEQ ID NO:39:	371
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 747 base pairs	
55	(B) TYPE: nucleic acid	
55	(C) STRANDEDNESS: double	
	•	

	(D) TOPOLOGY: circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
5	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
10	(A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
	(B) LOCATION 1747	
15		
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:	
	GTGAGCTATG ACAACACCGA TGATTATTAT TTCCCTAGAA ATGGGGTTAT CTTTAGTTCC	60
20	TATGCGACAA TGTCTGGTTT GCCAAGCTCT GGCACGCTCA ATTCTTGGAA CGGGTTAGGC	120
20	GGGAATGTCC GTAACACCAA AGTTTATGGT AAATTCGCCG CTTACCACCA TTTGCAAAAA	180
	TATTTATTGA TAGATTTGAT CGCTCGTTTT AAAACGCAAG GGGGCTATAT CTTTAGGTAT	240
	AACACCGATG ATTACTTGCC CTTAAACTCC ACTTTCTACA TGGGGGGCGT AACCACGGTG AGAGGCTTTA GGAACGGCTC AATCACACCT AAAGATGAGT TTGGCTTGTG GCTTGGAGGC	300
	GATGGGATTT TTACCGCTTC TACTGAATTG AGCTATGGGG TGTTAAAAGC GGCTAAAATG	360
25	CGTTTAGCGT GGTTTTTTGA CTTTGGTTTC TTAACCTTTA AAACCCCAAC TAGGGGGAGT	420
-	TTCTTCTATA ACGCTCCCAC CACGACGGCG AATTTTAAAG ATTATGGCGT TGTAGGGGCT	540
	GGGTTTGAAA GGGCGACTTG GAGGGCTTCT ACAGGCTTAC AGATTGAATG GATTTCGCCC	600
•	ATGGGGCCTT TGGTGTTGAT TTTCCCTATA GCGTTTTTCA ACCAATGGGG CGATGGCAAT	660
	GGCAAAAAAT GTAAAGGGCT GTGCTTTAAC CCTAACATGA ACGATTACAC GCAACATTTT	720
30	GAATTTTCTA TGGGAACAAG GTTTTAA	747
	(2) INFORMATION FOR SEQ ID NO:40:	
	(i) CRANENCE CHARACTERICO	
35	(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 1008 base pairs	
,,	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
	(2)	
10	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
15		
	(vi) ORIGINAL SOURCE:(A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	
50	(A) NAME/KEY: misc_feature	
	(B) LOCATION 11008	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:	
55	GTGCAACACT TCAATTTCCT CTATAAAGAT TCTTTATTTT CTATCGCTTT ATTCACTTTC	60

	ATTATCGCTC TTGTGATTTT ATTAGAACAG GCTAGAGCGT ATTTCACCCG AAAGAGAAAC	120
	AAAAAATTTT TGCAAAAATT CGCCCAAAAT CAAAACGCCT ATGCGAGCAG CGAGAATTTA	180
	GACGAGCTTT TAAAGCATGC TAAAATTTCC AGTTTGATGT TTTTAGCTAG GGCGTATTCT	240
	AAAGCGGATG TGGAAATGAG CATTGAAATC TTAAAAGGGC TTTTGAATCG CCCCTTAAAA	300
5	GATGAAGAAA AAATCGCTGT TTTAGATTTA TTGGCTAAAA ATTATTTTAG CGTGGGGTAT	-
-	TTGCAGAAAA CAAAAGACAC CGTGAAAGAA ATTTTGCGCT TTTCCCCAAG GAATGTGGAA	360
	GCGTTGTTGA AGCTTTTGCA TGCGTATGAA TTAGAAAAAG ATTATTCAAA GGCTTTAGAA	420
	ACCITICAN GUITIGAN IGCGIAIGAN TTAGAAAAAAG ATTATTCAAA GGCTTTAGAA	480
	ACTTTGGAAT GTTTGGAAGA ATTAGAGGTG CCTAAAATTG AAACGATTAA AAATTACCTC	540
10	TATTTAATGC ATTTAATAGA GAATAAGGAA GATGCGGCTA AAATCTTGCA TGTTTCAAAA	600
10	GCGTCGTTAG ATTTGAAAAA AATCGCTCTG AATCACTTAA AATCGCATGA TGAAAATCTT	660
	TTTTGGCAAG AAATTGATAC AACCGAACGG CTAGAAAATG TGATCGATCT TTTATGGGAT	720
	ATGAATATCC CTGCTTTTAT TTTAGAAAAA CATGCCCTTT TGCAGGACAT CGCGCGATCT	780
	CAAGGGTTGC TTTTGGATCA CAAACCTTGC CAAATTTTTG AATTAGAGGT TTTACGCGCT	840
	CTATTGCATA GCCCTATAAA AGCGAGTCTG ACTTTTGAAT ACCGCTGCAA GCATTGCAAA	900
15	CAAATCTTTC CTTTTGAAAG CCATAGGTGT CCTGTGTGTT ACCAGTTAGC GTTTATGGAT	
	ATGGTGCTTA AAATCTCTAA AAAAACGCAT GCTATGGGAG TGGATTAA	960
	THE PROCESS OF THE OWNER OWNER OF THE OWNER OWNE	1008
	(2) INFORMATION FOR SEQ ID NO:41:	
	(2) INFORMATION FOR SEQ ID NO:41:	
20	(-) aparmage and a second	
20	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1242 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
25		
	(ii) MOLECULE TYPE: DNA (genomic)	
	4.1.4.3	
	(iii) HYPOTHETICAL: NO	
	(111) HYPOTHETICAL: NO	
30		
30	(iv) ANTI-SENSE: NO	
30	(iv) ANTI-SENSE: NO	
30	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:	
30	(iv) ANTI-SENSE: NO	
	<pre>(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:</pre>	
30 35	<pre>(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:</pre>	
	<pre>(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:</pre>	
	<pre>(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:</pre>	
	<pre>(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:</pre>	
35	<pre>(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:</pre>	•
	<pre>(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:</pre>	•
35	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:	
35	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:	60 120
35	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:	120 180
35	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:	120 180
35	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:	120 180 240
35	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:	120 180 240 300
35	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:	120 180 240 300 360
35	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:	120 180 240 300 360 420
35	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 11242 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:41: ATGAGGAAAA TTTTTTCTTA TATTTCTAAG GTTCTATTAT TTATTGGGGT GGTTTATGCA GAGCCTGATT CTAAAGTGGA AGCCTTAGAA GGGAGGAAGC AAGAGTCTTC TTTGGATAAA AAAATCCGCC AAGAATTGAA GAGTAAGGAA TTGAAGAATA AGGAATTAAA GAATAAGGAT TTGAAAAATA AAGAAGAAAA GAAAGAAA	120 180 240 300 360 420 480
35 40 45	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 11242 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:41: ATGAGGAAAA TTTTTTCTTA TATTTCTAAG GTTCTATTAT TTATTGGGGT GGTTTATGCA GAGCCTGATT CTAAAGTGGA AGCCTTAGAA GGGAGGAAGC AAGAGTCTTC TTTGGATAAA AAAATCCGCC AAGAATTGAA GAGTAAGGAA TTGAAGAATA AGGAATTAAA GAATAAGGAT TTGAAAAATA AAGAAGAAA GAAAGAAA	120 180 240 300 360 420
35	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:	120 180 240 300 360 420 480
35 40 45	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:	120 180 240 300 360 420 480 540
35 40 45	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 11242 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:41: ATGAGGAAAA TTTTTTCTTA TATTTCTAAG GTTCTATTAT TTATTGGGGT GGTTTATGCA GAGCCTGATT CTAAAGTGGA AGCCTTAGAA GGGAGGAAGC AAGAGTCTC TTTGGATAAA AAAATCCGCC AAGAATTGAA GAGTAAGGAA TTGAAGAATA AGGAATTAAA GAATAAGGAT TTGAAAAATA AAGAAGAAAA GAAAGAAA	120 180 240 300 360 420 480 540 600
35 40 45	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 11242 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:41: ATGAGGAAAA TTTTTTCTTA TATTTCTAAG GTTCTATTAT TTATTGGGGT GGTTTATGCA GAGCCTGATT CTAAAGTGGA AGCCTTAGAA GGGAGGAAGC AAGAGTCTC TTTGGATAAA AAAAATCCGCC AAGAAATGAA GAAAGAAACA AAGACCAAGA GAAAAACCCAG AGCAGAAAT TCCCACTCCA AAGATCAAC GAAAACCCAG AGCAGAAAT AAGAACAACAGC CTCCTAAAAT CAAAGGGAGT ACTACTGGA AAGAAATAAA AAGAACAACCCCTC AAGCTACTGA AAAAAATAAG GAAACAACCCCTC AAGCTACTGA AAAAAATAAG GAAACAACCCCTC AAGCTACTGA AAAAAATAAG GAAACAACCCCTC AAGCTACTAA ACCACCCTTG AAGATAAGGT CTTGTTAATGA CGCTCACCAC AACACCCCTTG AAGATAAGGT CGTAGGGGGC AACAACCAAGA TCCCACTAACA ACCACCCTTG AAGATAAGGT CGTAGGGGGC AACAACTAAAA TCCAAGAA ACCACCTTTA AACACACCC CAAGAAATTG AGCCCTTAAAA AATCCAAGAA GAATGGCC CAAGAAATTG AGCCCTTAAAA AATCCAATGA GATCATTCA AACCACCAA AGCAACCCAA AACACCCATTA AACACACCAA AGCAACCCAA AGAAATTGA AACCCATTAA AACTCCATGTA GATGATTGCA AGCAATCCAA AGAATTGCCA AGAAATTGCA AACACCCATT AAACAGACCAT TAAGAATCCAA AGAATTGCAA GAAATTGCAACCA AACACCCATTT AACAGACCAAT TAAGAATCCAA AGAATTGCAA AGAATTGCAA AGAATTGCAACCA AACACCCATTT TAAGAATCCAA AGAATTGCAACCAA AGAATTGCAACCAA AACACCCATTT TAAGAATCCAA AGAATTGCAACCAA AACACCCATTT TAAGAATCCAA AGAATTGCAACCAA AACACCCATTT TAAGAATCCAA AGAATTGCAACCAA AACACCCATTT TAAGAATCCAA AGAATTGCAACCAA AGAATTGCAACCAA AACACCCATTT TAAGAATCCAACAACACCAA AGAATTGCAACCAACAACCAACCAACCAACCAACCAACAACCAAC	120 180 240 300 360 420 480 540 600 660
35404550	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 11242 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:41: ATGAGGAAAA TTTTTTCTTA TATTTCTAAG GTTCTATTAT TTATTGGGGT GGTTTATGCA GAGCCTGATT CTAAAGTGGA AGCCTTAGAA GGGAGGAAGC AAGACTCTTC TTTGGATAAA GAATAAGGAT TTGAAAAATA AGGAATTGAA GAGTAAGGAA TTGAAAAATA AGGAATTAAA GAATAAGGAT TTGAAAAATA AAGAAGAAAA GAAAGAACAAA AAAGCCAAGA GAAAACCCAG AGCAGAAGTC CATCATGGGG ACGCCAAAAA TCCCACTCCA AAGATCACGC CTCCTAAAAT CAAAGGGAGT ACAACCCCTC AAGCTACAAA AGGCGTTCAA AACACCCGC CAAAAACCTGA AGAAAAAGAT ACAACCCCTC AAGCTACTAA AAAAAATAAG GAAACAAGCC CTAGCTCTA AGAAAAAGAT ACAACCCCTC AAGCTACTAA AAAAAATAAG GAAAAAAGAT CCAAAAGGGGGC ATTCTAATAA CGCTACCAAC AACACCCTTG AAGATAAGGT CGTAGGGGGC ATTCTAATAA TCCACTATTA ACCCACTTTGA ACAACCCCTTG AAAATCCAAGA AGACCAAGAA TCCCATGTAA AACACCCTTG AAAATCCAAGA AGAGCAAGAA AGACCATTTCA AGACTAAGAC CATTAAAAAC CAAGAAATTG AGCGCTTAAAA AATCCAATGA AACACAACAC	120 180 240 300 360 420 480 540 600 660 720
35 40 45	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 11242 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:41: ATGAGGAAAA TTTTTTCTTA TATTTCTAAG GTTCTATTAT TTATTGGGGT GGTTTATGCA GAGCCTGATT CTAAAGTGGA AGCCTTAGAA GGGAGGAAGC AAGAGTCTC TTTGGATAAA AAAATCCGCC AAGAATTGAA GAGTAAGGAA TTGAAGAATA AGGAATTAAA GAATAAGGAT TTGAAAAATA AAGAAGAAAA GAAAGAAA	120 180 240 300 360 420 480 540 600 660 720 780

5	AGTAAGGCCA ATGAAAAAAT AGAGATGAAA ACCCTAAACC CTCAAATCGC CCAAGTCTTT 10 ATTTCGCATG AGCAAGGCTC TTTCACGCCC GTTATGAATG GGGGTGGGGG GCAGTTCATC 10 ACCTTTTATA TCAAGGAAAA AAGGGGTAAA AATGAAGTGA GCTTCAGTCA GGCCAAGCAA 11	20 80 40
•		42
	(2) INFORMATION FOR SEQ ID NO:42:	•
10	 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 561 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular 	
15		
	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
20	(iv) ANTI-SENSE: NO	
	<pre>(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori</pre>	
25	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1561</pre>	
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:	
	GTGAATGGGT TTTTCATGGG TGCGGGTTAT CAACAAGGTC GTTATGGCCC TTATAACAGC 1 AATTACTCTG ATTGGCGTCA TGGCAATGAC CTTTATGGTT TGAATTTCAA ATTAGGTTTT 1	60 20 80
35		40 00
	ATTGTCAATC TCATTCCTTT GGATAAATTC GCTCTAGGTC TCATTGGTGG CGTTCAATTA 3	60 20
	AATTTAGGCG GAAGAATGCG TGTTGGGGAT CGCAGTGCGT TTGAAGCGGG CGTGAAATTC 4	80
40		40 61
	(2) INFORMATION FOR SEQ ID NO:43:	
•	(i) SEQUENCE CHARACTERISTICS:	
45	(A) LENGTH: 729 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double	
50	(D) TOPOLOGY: circular	
J U	(ii) MOLECULE TYPE: DNA (genomic)	٠
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	

480

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(vi) ORIGINAL SOURCE:
            (A) ORGANISM: Helicobacter pylori
          (ix) FEATURE:
 5
                (A) NAME/KEY: misc_feature
                (B) LOCATION 1...729
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:
     ATGAAAAAT TTTTTCTCA ATCTTTGTTA GCTCTTATTA TCTCTATGAA TGCGGTATCT
     GGCATGGATG GTAATGGCGT TTTTTTAGGG GCGGGTTATT TGCAAGGACA GGCGCAAATG
                                                                          120
     CATGCGGATA TTAATTCTCA AAAACAAGCC ACCAACGCTA CGATCAAAGG CTTTGACGCG
                                                                          180
     CTCTTGGGGT ATCAATTTT CTTTGAAAAA CACTTTGGCT TACGCCTTTA TGGGTTTTTT
                                                                          240
     GACTACGCTC ATGCCAATTC TATTAAGCTT AAAAACCCTA ACTATAATAG CGAAGCGGCG
                                                                          300
     CAAGTGGCTA GTCAAATTCT TGGGAAACAA GAAATCAATC GTTTAACAAA CATTGCCGAT
                                                                          360
     CCCAGAACTT TTGAGCCGAA CATGCTCACT TATGGGGGGG CTATGGACGT GATGGTTAAT
                                                                          420
     GTCATCAATA ACGGCATCAT GAGTTTGGGG GCTTTTGGCG GGATACAATT GGCCGGCAAT
                                                                          480
     TCATGGCTTA TGGCGACACC GAGCTTTGAG GGCATTTTAG TGGAACAAGC CCTTGTGAGC
                                                                          540
     AAGAAAGCCA CTTCTTTCCA ATTTTTATTC AATGTGGGGG CTCGCTTAAG GATCTTAAAA
                                                                          600
     CATTCTAGCA TTGAAGCGGG CGTGAAATTC CCCATGCTAA AGAAAAACCC CTACATCACT
                                                                          660
     GCAAAAAATT TGGATATAGG GTTTAGGCGC GTGTATTCGT GGTATGTGAA TTACGTGTTC
                                                                          720
     ACTTTCTAG
                                                                          729
     (2) INFORMATION FOR SEQ ID NO:44:
25
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 771 base pairs
               (B) TYPE: nucleic acid
               (C) STRANDEDNESS: double
30 -
               (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
        (iii) HYPOTHETICAL: NO
35
         (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
40
         (ix) FEATURE:
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...771
45
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:
     ATGGGATACG CAAGCAAATT AGCTTTAAAG ATTTGTTTGG TAGGTTTATG TTTATTTAGC
     ACCCTTGGTG CAGAACACCT TGAGCAAAAA GGGAATTATA TTTATAAGGG AGAGGAGGCT
     TATAATAATA AGGAATATGA GCGAGCGGCT TCTTTTTATA AGAGCGCTAT TAAAAATGGT
                                                                         180
50
    GAGTCGCTTG CTTATATTCT TTTAGGGATC ATGTATGAAA ATGGTAGGGG TGTACCTAAA
                                                                         240
     GATTACAAGA AAGCGGTTGA ATATTTCCAA AAAGCTGTTG ATAACGATAT ACCTAGAGGG
                                                                         300
     TATAACAATT TGGGCGTGAT GTATAAAGAG GGTAAGGGAG TTCCTAAAGA TGAAAAGAAA
                                                                         360
     GCGGTGGAAT ATTTTAGAAT AGCTACAGAG AAAGGTTATA CTAACGCTTA TATCAACTTA
                                                                         420
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GGCATCATGT ATATGGAGGG CAGGGGAGTT CCAAGTAACT ATGCGAAAGC GACAGAATGT

TTTAGAAAAG CGATGCATAA GGGCAATGTG GAAGCTTATA TTCTCCTAGG GGATATTTAT

TATAGCGGGA ATGATCAATT GGGTATTGAG CCGGACAAAG ATAAGGCTGT TGTCTATTAT AAAATGGCGG CTGATGTGAG TTCTTCTAGA GCTTATGAAG GGTTGTCAGA GTCTTATCGG TATGGGTTAG GCGTGGAAAA AGATAAAAAA AAGGCTGAAG AATACATGCA AAAAGCATGC GATTTTGACA TTGATAAAAA TTGTAAGAAA AAGAACACTT CAAGCCGATA A	600 660 720 771
(2) INFORMATION FOR SEQ ID NO:45:	
(:) GROUPING GUADA GEODA CONTOC	
(i) SEQUENCE CHARACTERISTICS:	
(A) LENGTH: 1974 base pairs (B) TYPE: nucleic acid	
(C) STRANDEDNESS: double	
(D) TOPOLOGY: circular	
(ii) MOLECULE TYPE: DNA (genomic)	
(iii) HYPOTHETICAL: NO	•
(iv) ANTI-SENSE: NO	
(IV) ANII-SENSE. NO	
(vi) ORIGINAL SOURCE:	
(A) ORGANISM: Helicobacter pylori	
(ix) FEATURE:	
(A) NAME/KEY: misc_feature (B) LOCATION 11974	
(B) LOCATION 11974	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:	
ATGAGAAAAC TATTCATCCC ACTTTTATTA TTCAGCGCTT TAGAAGCGAA CGAGAAAAAC	60
GGCTTTTCA TAGAAGCCGG CTTTGAAACT GGGCTATTAG AAGGCACACA AACGCAAGAA	120
AAAAGACACA CCACCACAAA AAACACTTAC GCAACTTACA ATTATTTACC CACAGACACG	180
ATTTTAAAAA GAGCGGCTAA TTTATTCACC AATGCCGAAG CGATTTCAAA ATTAAAATTC	240
TCATCTTTAT CCCCTGTTAG AGTGTTGTAT ATGTATAATG GTCAATTAAC TATAGAAAAC	300
TTCTTGCCTT ATAATTTAAA TAATGTTAAG CTTAGTTTTA CAGACGCTCA AGGCAATGTG	360
ATCGATCTAG GCGTGATAGA GACTATCCCC AAACACTCTA AGATTGTTTT GCCCGGAGAG	420
GCATTTGATA GTCTAAAAAT TGACCCCTAT ACTTTATTTC TTCCAAAAAT TGAAGCCACT	480
AGCACTTCTA TTTCTGACGC TAACACGCAG AGGGTGTTTG AAACGCTCAA TAAGATTAAG	540
ACAAATTTGG TCGTAAATTA TAGGAATGAA AACAAATTTA AAGATCACGA AAATCATTGG	600
GAAGCCTTTA CCCCACAAAC CGCAGAAGAA TTCACTAATT TAATGTTGAA CATGATCGCT GTTTTAGACT CCCAATCTTG GGGCGATGCG ATCTTAAACG CTCCTTTTGA GTTCACTAAC	660
AGCCCAACAG ATTGCGATAA TGATCCTTCA AAATGCGTAA ATCCTGGGAC AAACGGGCTT	720
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AAAAACAAAG CGGATCTTGA TGTAATTGTT TTAAAGGATT CAGGGGTTGT AGGGCTTGGG	
AGTGATATTA CCCCTAGCAA CAATGATGAT GGCAAGCATT ATGGCCAGTT AGGGGTAGTA	
GCTTCTGCTT TAGATCCTAA AAAACTCTTT GGCGATAACC TTAAGACTAT CAATTTAGAG	
GATTTAAGAA CCATCTTGCA TGAATTCAGC CACACTAAAG GCTATGGGCA TAACGGGAAT	
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AAGCCAAAAG ATTCTGATGG CCTCCCCTAT AATGTGTGTT CGCTTTATGG GGGATCCAAT	
CAGCCCGCTT TCCCTAGCAA CTACCCTAAT TCCATCTATC ACAATTGTGC GGATGTCCCG	
	1200

CCGATCAACT ACGCTAACTT GGGGAGTCAA ACAAACTACA ACCTAAACGC TAGTTTAAAC

ACGCAAGATT TAGCCAATTC CATGCTCAGC ACCATCCAAA AAACCTTTGT AACTTCTAGC

GTTACCAACC ACCATTTTC AAACGCATCG CAAAGTTTTA GAAGCCCTAT TTTAGGGGTT

AACGCTAAAA TAGGCTATCA AAACTACTTT AATGATTTCA TAGGGTTGGC TTATTATGGC

ATCATCAAAT ACAATTACGC TAAAGCTGTT AATCAAAAAG TCCAGCAATT GAGCTATGGT

5	GGGGGGATAG ATTTGTTATT GGATTTCATC ACCACTTACT CCAATAAAAA TAGCCCTACA GGCATTCAAA CCAAAAGGAA TTTTTCTTCA TCTTTTGGTA TCTTTGGGG GTTAAGGGC TTGTATAACA GCTATTATGT GTTGAACAAA GTCAAAGGAA GCGGCAATTT AGATGTGGCT ACCGGGTTGA ACTACCGCTA TAAGCATTCT AAATATTCTG TAGGGATTAG CATCCCTTTA	1680 1740 1800 1860
	ATCCAAAGAA AAGCTAGCGT CGTTTCTAGC GGTGGCGATT ATACGAACTC TTTTGTTTTC AATGAAGGGG CTAGCCACTT TAAGGTGTTT TTCAATTACG GGTGGGTGTT TTAG	1920 1974
	(2) INFORMATION FOR SEQ ID NO:46:	
10	(i) SEQUENCE CHARACTERISTICS:	
. •	(A) LENGTH: 504 base pairs (B) TYPE: nucleic acid	
• .	(C) STRANDEDNESS: double	
15	(D) TOPOLOGY: circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
20	(iv) ANTI-SENSE: NO	
	<pre>(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori</pre>	
25	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1504</pre>	
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:	
,	ATGAAATTGG TGAGTCTTAT TGTAGCGTTA GTTTTTTGTT GTTTTTTAGG GGCTGTAGAG TTGCCTGGAG TTTATCAAAC TCAAGAATTT TTATACATGA AAAGCTCTTT TGTGGAGTTT	60 120
	TTTGAGCATA ACGGGAAGTT CTATGCCTAT GGTATTTCTG ATGTGGATGG CTCTAAAGCC AAAAAAGACA AACTCAATCC TAACCCAAAG CTAAGGAATC GCAGCGATAA AGGCGTGGTG	180 240
35	TITITAAGCG AITTGATTAA GGTTGGGGAA CAATCTTATA AAGGCGCTAA GCCGCTAAA	300
	TTTTATGACG GCAAGACCTA CCATGTGAGA GTCACTCAAA ATTCAAACGG GGATTTGGAA TTCACTTCAA GCTATGACAA ATGGGGGTAT GTGGGCAAAA CCTTCACCTG GAAACGCCTG	360 420
•	AGCGATGAAG AAATCAAAAA TCTAAAGCTC AAGCGTTTTA ACTTGGACGA AGTCCTTAAA ACCCTCAAAG ATAGCCCTAT TTAA	480
40		504
	(2) INFORMATION FOR SEQ ID NO:47:	
45	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 885 base pairs	
43	(B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular	
50	(ii) MOLECULE TYPE: DNA (genomic)	
•	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
55	(vi) ORIGINAL SOURCE:	

180

240

300

360

420

(A) ORGANISM: Helicobacter pylori

(ix) FEATURE: (A) NAME/KEY: misc feature 5 (B) LOCATION 1...885 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:47: ATGAGTAATC AAGCGAGCCA TTTGGATAAT TTTATGAACG CTAAAAATCC CAAAAGTTTT 60 TTTGATAATA AGGGGAATAC CAAATTCATC GCTATCACAA GCGGTAAGGG GGGCGTGGGG AAATCCAACA TTAGCGCTAA TTTAGCTTAC TCTTTATACA AGAAAGGTTA TAAGGTAGGG GTATTTGATG CGGATATTGG TTTAGCGAAT TTAGATGTCA TTTTTGGGGT GAAAACCCAT AAAAATATCT TGCATGCCTT AAAAGGCGAA GCCAAATTGC AAGAAATCAT TTGCGAGATT GAACCCGGGC TTTGCTTAAT CCCTGGGGAT AGCGGCGAAG AAATTTTAAA ATACATCAGC GGCGCGGAAG CTTTGGATCG ATTCGTAGAT GAAGAGGGGG TTTTAAGCTC TTTAGATTAT 420 ATTGTGATTG ATACGGGTGC TGGGATTGGG GCCACTACGC AAGCGTTTTT GAATGCGAGC 480 GATTGCGTGG TGATTGTTAC CACACCCGAT CCTTCAGCGA TTACCGATGC GTATGCATGC 540 ATTAAAATCA ACTCCAAGAA TAAAGATGAA TTGTTCCTTA TCGCTAACAT GGTAGCCCAA 600 CCTAAAGAAG GCAGGGCGAC TTATGAAAAG CTATTCAAGG TGGCTAAAAA CAATATCGCT 660 TCATTAGAAT TGCACTATTT AGGGGCGATT GAAAACAGCT CCTTATTGAA ACGCTATGTG 720 AGGGAGCGAA AGATTTTGAG GAAAATAGCC CCTAACGATT TGTTTTCGCA ATCCATTGAC 780 CAGATAGCGA GCCTTTTAGT TTCTAAACTA GAAACCGGCA CTTTAGAAAT ACCAAAAGAA 840 GGTTTAAAAA GCTTTTTTAA AAGGCTTTTG AAGTATTTGG GGTAG 885 25 (2) INFORMATION FOR SEQ ID NO:48: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1119 base pairs (B) TYPE: nucleic acid 30 (C) STRANDEDNESS: double (D) TOPOLOGY: circular (ii) MOLECULE TYPE: DNA (genomic) 35 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 40 (A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1...1119 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:48: TTGGAACCTT CAAGAAATCG CCTAAAACAT GCCGCCTTTT TTGTGGGGCT TTTTATCGTT TTGTTTTAA TTATAATGAA GCACCAAACC TCCCCCTATG CTTTCACGCA TAATCAAGCC

CTTGTCACTC AAACCCCCCC CTATTTCACG CAACTCACTA TCCCTAAACC AAATGACGCT

TTAAGCGCGC ATGCGAGCTC TTTAATCAGC TTGCCTAACG ACAATCTTTT GAGCGCTTAT

TTTAGCGGCA CTAAAGAAGG GGCAAGGGAT GTGAAAATCA GCGCGAATCT TTTTGACAGC

AAGACTAATC GCTGGAGCGA AGCCTTCATT CTTTTAACCA AAGAAGAGCT TTCTCATCAT

TCGCATGAAT ACATCAAAAA ATTAGGTAAC CCCTTGCTTT TTTTGCATGA TAATAAAATT

TTGTTGTTTG TCGTAGGGGT GAGCATGGGC GGGTGGGCCA CTTCTAAAAT CTATCAATTT

5	GAAAGCGCTT TAGAGCCGAT TCATTTAAG TTTGCGCGAA AACTCTCTTT AAGCCCTTTT TTAAATTTGA GCCATTAGT AAGGAATAAG CCTTTAAACA CCACTGATGG CGGGTTTATG CTACCACTCT ATCACGAATT AGCCCACCAA TACCCCTTGT TGTTGAAATT TGACCAACAA AATAACCCAA GAGAGCTTTT AAGGCCTAAT ACCTTAAACC ACCAGCTCCA ACCAAGCTTA ACCCCCTTTA AAGACTGCGC TGTCATGGCG TTTAGAAACC ATTCTTTAAA AGATAGCCTC ATGCTAGAAA CCTGTAAAAC CCCCACTGAT TGGCAAAAAC CCATTTCTAC AAATCTTAAA AACTTAGATG ATTCTTTAAA TTTACTCAAT TTAAATGGAA TATTGTATTT GATCCACAAC CCTAGCGATT TATCACTGCG TCGTAAAAGAA CTTTGGCTTT CTAAATTAGA AAACTCCAAC CCTTAAATCCGC ATTTTATAGA TTTGGATAAA GCGAATGAAG TGAGTTACCC AAGCTATAGC CTTAATCCGC ATTTTATAGA TATTGTCTAT ACTTACAACC GCTCTCATAT CAAACACATC	540 600 660 720 780 840 900 960 1020 1080 1119
	(2) INFORMATION FOR SEQ ID NO;49:	
15	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 2937 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double	
20	(D) TOPOLOGY: circular	
. 20	(ii) MOLECULE TYPE: DNA (genomic)	•
	(iii) HYPOTHETICAL: NO	
25	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
30	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 12937</pre>	
35	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:	٠
	ATGAAGAAAA GAAAACATGT ATCCAAGAAA GTGTTTAATG TCATTATCTT GTTTGTGGCA	60
	GTATICACIC TITIAGTCGT CATTCACAAA ACCCTTTCAA ACGCCATTCA CATACAAAAT	120
	TIAAAAATIG GAAAACTTGG CATTTCTGAA TTATACTTAA AACTCAATAA CAAGCTTTCT	180
40	TIGGAAGTIG AGCGGGITGA TCTCTCTTCT TTCTTCCATC AAAAACCCAC TAAAAAGCGT	240
-10	TTAGAAGTTT CTGATTTGAT TAAAAATATC CGTTATGGCA TTTGGGCGGT GTCTTATTTT	- 300
	GAAAAACTTA AAGTCAAAGA AATCATTTTA GACGATAAAA ATAAAGCCAA TATCTTTTTT	360
•	GATGGGAATA AATACGAGTT AGAATTTCCA GGAATCAAAG GGGAATTTTC CCTAGAAGAC GATAAAAATA TCAAGCTTAA AATCATCAAT TTGCTTTTTA AAGATGTTAA AGTCCAAGTG	420
	GATGGCAACG CCCACTATTC ACCCAAAGCC AGGAAAATGG CGTTCAATTT GATTGTCAAG	480
45	CCCTTAGTTG AACCCAGCGC TGCAATTTAT TTGCAAGGGC TAACCGATTT AAAAACCATA	540
	GAATTAAAAA TTAACACTTC TCCAATGAAA AGCCTAGCGT TTTTAAAGCC TCTTTTCCAA	600 660
	CGCCAATCGC AAAAAAATTT AAAAACGTGG ATTTTTGACA AGATCCAATT TGCCAGCTTT	720
	AAGATTGATA ACGCTTTAAT CAAGGCTAAT TTCACTCCTA GCGAGTTTAT CCCATCCCTT	780
. en	TIGGAAAATI CIGTAGITAA AGCCACTIIG ATTAAGCCII CAGICGIITI TAATGAIGGC	840
- 50	TTATCGCCCA TTAAAATGGA TAAAACCGAA TTGATTTTCA AAAACAAACA GCTCCTCATA	900
	CAGCCCCAAA AAATCACTTA TGAAACCATG GAATTAACCG GCTCTTACGC CACTTTTTCC	960
	AATTIGTIAG AAGCCCCTAA GTTGGAGGTT TTTTTAAAAA CGACCCCTAA TTATTATGCC	1020
	GATAGCATTA AGGATTTATT GAGCGCTTAT AAAGTCGTTT TACCTTTGGA TAAAATCAGC	1000
55	ATGCCATCTA GCGCGGATTT GAAGCTCACT TTGCAATTCT TAAAAAACAC CGCCCCCTTA	1140
"	TTTAGCGTTC AAGGCAGCGT TAATTTGCAA GAAGGCACTT TCTCGCTCTA TAATATCCCC	1200

60

120

	•		•				
	CTTTACACGC	AAAGCGCTCA	AATCAATTTG	GACATCGCCC	AAGAATACCA	ATACATCTAC	1260
						AATCGCTTTA	1320
		AAAAAAACCT					1380
		TCAACATGCG					1440
5						AAATTCAGAA	
		GAAAAATCAT					1560
		ACGCCACAGG					1620
		ACATACAATG					1680
		CTTTTAAGAT					
10		CCCTAAAAGA					1740
10		CTAAAGATTT					1800
		TTTCTTTATT					1860
							1920
						TAATAACATT	
15		TTGATGATTT					2040
13						TTTCATTAGC	2100
		GCTATGAAAA					2160
		TGCTGATCTA					2220
		ATAGGGTGAA					2280
20		GGGCTTTGTA					2340
20		AAGATTTCGT					2400.
		ATGGCGAATT					2460
		TCAATCTCAT					2520
		ATGGCTATCA					2580
25		TAGAAAAAAT					2640
25		TAGACAAAA					2700
•		TCTTAAATAA					2760
						CCAAGTAACT	2820
						CACGCCTATT	2880
20	GACATCATCG	TGGATGAAGT	CAAGAAAAAC	ATTGATTCAA	AAAGGAAATT	AAAATGA	2937
30	(2) THEODM	ATION FOR SE	O TO MOLEO				
	(Z) INFORM	TION FOR SI	OC.ON GI GE	•		•	
	/i) S	EQUENCE CHAP) A CT FD T CT T C				
		(A) LENGTH:				•	
35		(B) TYPE: nu	_	Jails			
		(C) STRANDEI					
•		(D) TOPOLOGY				•	
		(D) IOPOLOGI	. CIICUIAI			•	
	(ii) MC	OLECULE TYPE	. DNA (gene	omia)			
40	(11)	ADDCOLD IIII	. DIM (gene	mile)			
10	(iii) W	POTHETICAL:	NO	•			
	(III) H	POINEIICAL:	NO				
	(iv) AN	NTI-SENSE: N	īO	•			•
•	(IV) AL	III-BENBE: N					
45	/rri) OT	RIGINAL SOUR	CF.		•		
43		(A) ORGANISM					
	,	(A) ORGANISM	: Helicobac	cer pylori			
	(ix) FE	ים מדוייית ל					
•			'. miga fort				
50		(A) NAME/KEY (B) LOCATION	_	.ure			
50	•	(B) INCATION	1 11434	*			
	/ \ CT	OTENICE DECC	ים דחשדראי פי	0 TD NO 50		•	
	(XI) SE	EQUENCE DESC	KIPITON: SE	7 אָס: אָס: אַס: אַס:			

ATGAATACTA TTATAAGATA TGCGAGTTTA TGGGGCTTGT GTATTACTCT AACTCTAGCG

CAAACCCCCT CTAAAACCCC TGATGAAATC AAGCAAATCC TTAACAATTA TAGCCATAAG

	AATTTAAAGC TCATTGATCC GCCGACAAGT TCTTTAGAAG CGACACCGGG TTTTTTACCC	180
	TCGCCTAAAG AAACAGCGAC CACGATCAAT CAAGAGATCG CTAAATACCA TGAAAAAAGC	240
	GATAAAGCCG CTTTGGGGCT TTATGAATTG CTAAAGGGGG CTACCACCAA TCTCAGTTTG	300
_	CAAGCGCAAG AACTCAGTGT CAAGCAAGCG ATGAAGAACC ACACCATCGC CAAAGCGATG	360
5	TTTTTGCCTA CTTTGAACGC GAGTTATAAT TTTAAAAATG AAGCTAGGGA TACTCCAGAA	420
•	TATAAGCATT ATAACACCCA ACAACTCCAA GCTCAAGTCA CATTGAATGT GTTTAATGGC	480
•	TTTAGCAATG TGAATAATGT CAAAGAAAAG TCTGCGACTT ACCGATCCAC TGTGGCTAAT	540
	TTAGAATATA GCCGCCAAAG CGTGTATTTG CAAGTGGTGC AACAATACTA CGAGTATTTT	600
*	AACAATCTCG CTCGCATGAT CGCTTTGCAA AAGAAATTAG AGCAAATCCA AACGGACATT	660
10	AAAAGGGTTA CTAAGCTCTA TGACAAAGGG CTGACCACGA TTGATGATTT ACAAAGCTTA	720
	AAAGCGCAAG GGAATTTGAG CGAATACGAT ATTTTGGACA TGCAATTTGC TTTGGAGCAA	780
	AACCGCTTGA CTTTAGAATA CCTCACTAAC CTCAGTGTGA AAAATTTGAA AAAGACCACG	840
	ATTGATGCGC CTAATTTGCA ATTAAGAGAA AGGCAGGATT TGGTTTCTTT AAGGGAGCAG	900
	ስጥጥርጥርርስር ጥርእርእጥእርርእ እእእርእእርርእእ ር መርእ እመከተመ እርርእር እና እ	960
15	CACTOATCCC TOTTOTTTCCAT CCAAAAACCC CCTTATCCA CCTTATCCA	020
	TACCCACCTC ACCAAAAAAC CCCTCCCCCTT ACTCCCC TO	080
	CCCTTCACCT TCCAAAAACA ATCCATCATCATCA CTACCCCAA T T T T	140
	CCCTATAAA AATTCCACCA ACAAAAAAA GAAAAA GAAAA	200
	CCCACACCTA ACATTCAATC TTCAAACCT ACTTTCAACCA	260
20	AATATTAAAA CCAAATTACCA CCCGAAGGGGA CGCGAAGGGA CGCGAAGGGA CGCGAAGGA CGCGAAGA CGCAAGA CAAGA CA	320
,	ACCACCCCC TOTCATCCACA ACTCCCTTA CARACTA ACTCC	380
	AAACCCAAPT ACATETTAA CACCCCCAB PRANCE CONTRACTOR CONTRA	434
25	(2) INFORMATION FOR SEQ ID NO:51: (i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1239 base pairs	
	(B) TYPE: nucleic acid	
30	(C) STRANDEDNESS: double	
30	(D) TOPOLOGY: circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
35	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
40	(A) ORGANISM: Helicobacter pylori	
40		
	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
	(B) LOCATION 11239	
45	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:	
	ATGCTATCTT TTATAAGCGC GTTTGATAAA AGGGGCGTTT CAATACGCCT TCTAACAGCC	60
	<u> እእስጥልሮሮሞሞሞ ሮሞአአአአለምሮአ አአአአለም ርአን በርርርምን መስጠ የተ</u>	20
50	TOTO ACARA ARCTOCOTAC CARROCCAM ARCCOMP	.80
		40
	TTCTCTCTAXX XXCTCCATCTC XXXCCCCXXXXXXXXXX	00
	CXXXXXCXXX XXXXXXXXXXXXXXXXXXXXXXXXXXX	60
	ATCATAAACC CCATTCAAAA CTATAAAA CAAAAA CAAAAA	20
55	ATTAAAAATT TAGAAAAAAA CAA COTOONIONN ACCON CONT.	80
	Service Continuit	40

- 127 -

	•	
	GCGATCGCCA AGTTAGAAAT TTTAAAATCG CTATTAGAAA TCCAAAAAAA CGATTTAGAA	600
-	GTAGCGCTCT CTAGCAGCCA TTATTCCATG GGCGAATTGA CTTTTAAAGA AAACGAGATT	660
•	TTAAGCATTG CCCCTAAAAA TTTTGAATTC AATAACGAGC AAGAGCTGCA TAACATTAGC	720
. 5	GCCACTAATT ACGATATTGC GATCGCCAGG CTTGATGAAG AAAAAGCACA AAAAGACATC	780
3	ACTCTGGCTA AAAAAAGCTT TTTAGAAGAC ATAAACGTTA CCGGGGTGTA TTATTTCCGC TCCAAACAAT ACTATAACTA CGACATGTTT AGCGTCGCTT TGTCTATCCC TTTACCTCTT	840
	TATGGCAAGC AGGCTAAATT AGTGGAGCAA AAGAAAAAAG AAAGCTTGGC GTTTAAAAGC	900 960
	GAAGTGGAAA ACGCCAAAAA CAAAACGCGC CACCTGGCCC TAAAACTCCT TAAAAAATTA	1020
-	GAAACCTTGC AAAAAAACCT GGAATCGATC AATAAAATCA TCAAACAGAA TGAAAAAAATC	1080
10	GCGCAAATTT ATGCGCTTGA TTTGAAAACT AATGGCGATT ACAACGCTTA TTACAACGCC	1140
	TTGAATGACA AAATCACTAT TCAAATCACC CAGCTTGAAA CCTTAAGCGC TCTAAATAGT	1200
	GCTTATTTGT CCTTACAAAA TCTCAAAGGA TTAGAATGA	1239
••	· · · · · · · · · · · · · · · · · · ·	
15	(2) INFORMATION FOR SEQ ID NO:52:	
13	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 414 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
20	(D) TOPOLOGY: circular	
-	(ii) MOLECULE TYPE: DNA (genomic)	
	(1211) WYDDWYDD DAY YD	
25	(iii) HYPOTHETICAL: NO	
23	(iv) ANTI-SENSE: NO	
	(IV) ANII DANDA. NO	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
30		
	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
	(B) LOCATION 1414	
35	(xi) SEQUENCE DESCRIPTION: SEO ID NO:52:	
	(iii) dagedied beschiff for. dag ib No. 32.	
	ATGCGTATAG TTAGAAATTT ATTTCTTGTA TCGTTTGTGG CGTATAGTAG TGCGTTCGCA	60
	GCGGATTTAG AAACCGGAAC CAAAAACGAC AAAAAGAGCG GTAAAAAAATT TTACAAACTC	120
40	CATAAAAACC ATGGCTCAGA AACCGAGACT AAAAACGATA AAAAGCTTTA TGATTTCACT	180
40	AAAAATAGCG GATTAGAAGG CGTGGATTTA GAAAAAAGCC CTAACCTTAA AAGCCATAAA	240
	AAAAGCGATA AAAAGTTTTA TAAACAACTC GCTAAAAACA ATATCGCTGA AGGGGTGAGC	300
	ATGCCGATTG TGAATTTCAA TAAAGCCCTA TCTTTTGGGC CTTATTTTGA AAGGACTAAA	360
•	AGCAAAAAA CCCAATACAT GGACGGCGGG TTGATGATGC ACATCCGTTT TTAA	414
45	(2) INFORMATION FOR SEQ ID NO:53:	
	(1) Interest for BEG 15 No.33.	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 930 base pairs	
	(B) TYPE: nucleic acid	
50	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
•	(ii) MOTECTITE TUDE. DNA (concris)	
	(ii) MOLECULE TYPE: DNA (genomic)	
55	(iii) HYPOTHETICAL: NO	

```
(iv) ANTI-SENSE: NO
        (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
                (B) LOCATION 1...930
10
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:
     TTGATGCCAC AAAACCAGCT TGTGATCACC ATCATTGATG AATCAGGCTC TAAGCAACTC
     AAATTTTCTA AAAATTTAAA ACGCAACCTC ATCATTCTG TTGTCATTCT TTTATTGATC
15 GTGGGGCTTG GCGTGGGGTT TTTAAAATTT TTAATCGCTA AAATGGATAC GATGACAAGC
                                                                         180
     GAGAGGAATG CGGTTTTAAG GGATTTTAGG GGTTTGTATC AAAAAAATTA CGCCCTAGCG
                                                                         240
     AAAGAGATTA AAAACAAGCG AGAAGAGCTT TTTATTGTGG GGCAAAAGAT CCGTGGGCTA
                                                                         300
     GAATCCTTGA TTGAAATCAA AAAGGGGGCT AATGGGGGGAG GGCATCTCTA TGATGAAGTG
                                                                         360
     GATTTAGAAA ATTTGAGCTT AAATCAAAAA CATTTAGCAC TCATGCTCAT TCCTAATGGC
                                                                         420
     ATGCCCCTAA AAACTTATAG CGCTATCAAA CCCACTAAAG AAAGGAACCA CCCCATTAAA
20
                                                                         480
     AAGATTAAGG GCGTTGAATC CGGGATCGAT TTTATCGCGC CATTGAACAC GCCTGTGTAT
     GCGAGCGCTG ATGGGATTGT GGATTTTGTG AAGACTCGTT CTAATGCGGG GTATGGGAAC
     TTGGTGCGCA TTGAACATGC GTTTGGTTTC AGCTCCATTT ATACGCACTT AGATCATGTC
     AATGTGCAGC CTAAAAGCTT CATCCAAAAA GGGCAGTTGA TTGGCTATAG CGGGAAGAGC
     GGTAATAGCG GCGGCGAAAA ATTGCATTAT GAAGTGCGGT TTTTGGGTAA AATTTTAGAC
     GCAGAAAAAT TCCTAGCATG GGATTTGGAT CATTTTCAAA GCGCTTTAGA AGAAAATAAA
     TTTATTGAAT GGAAGAATCT GTTTTGGGTT TTAGAAGACA TCGTCCAGCT CCAAGAGCAT
    GTGGATAAAG ACACCTTAAA AGGTCAGTAG
30
   (2) INFORMATION FOR SEQ ID NO:54:
         (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 999 base pairs
               (B) TYPE: nucleic acid
35
               (C) STRANDEDNESS: double
               (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
40
        (iii) HYPOTHETICAL: NO
       (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
45
              (A) ORGANISM: Helicobacter pylori
       (ix) FEATURE:
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...999
50
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:
    GTGCTATATT TTTTAACCAG TTTATTTATT TGCTCTTTGA TTGTTTTGTG GTCTAAAAAA
    TCCATGCTCT TTGTGGATAA CGCTAATAAA ATCCAAGGCT TCCATCATGC AAGAACCCCA
    CGAGCCGGGG GGCTTGGGAT CTTTCTTTCT TTTGCGTTGG CTTGTTATCT TGAACCTTTT
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	GAGATGCCTT TTAAGGGGCC TTTTGTTTTC TTAGGGCTAT CGCTAGTGTT TTTGAGCGGT	240
	TTTTTAGAAG ACATTAACCT TTCATTAAGC CCCAAAATAC GCCTTATTTT GCAAGCTGTA	300
	GGGGTCGTTT GCATCATTTC ATCAACGCCT TTAGTGGTGA GCGATTTTTC GCCCCTTTTT	360
	AGCTTGCCTT ATTTCATCGC TTTTTTATTC GCTATTTTTA TGCTGGTGGG TATCAGTAAC	420
5	GCTATTAATA TCATTGACGG GTTTAACGGG CTTGCATCTG GGATTTGCGC GATCGCGCTT	480
	TTAGTCATTC ATTATATAGA CCCTAGCAGT TTGTCTTGTT TGCTCGCTTA CATGGTGCTT	540
	GGGTTTATGG TGTTAAATTT CCCTTCAGGA AAGATTTTTT TAGGCGATGG GGGGGCGTAT	600
	TTTTTGGGTT TGGTGTGCGG GATTTCTCTC TTGCATTTGA GTTTGGAGCA AAAAATCAGC	660
	GTGTTTTTTG GGCTCAATTT AATGCTTTAT CCGGTCATAG AGGTGCTTTT TAGTATCCTT	720
10	AGGCGCAAAA TAAAACGCCA GAAAGCCACC ATGCCGGATA ATTTGCATTT GCACACCCTT	780
	TTATTTAAAT TCTTGCAACA ACGCTCTTTC AATTACCCTA ACCCTTTATG CGCGTTTATC	840
	CTTATTCTAT GCAACCTGCC TTTTATTTTA ATAAGCGTTT TGTTTCGCTT GGACGCTTAT	900
	GCGCTCATTG TGATTAGCCT AGTCTTTATC GCATGCTATT TAATAGGCTA TGCTTATTTG	960
	AATAGGCAAG TTTGCGCTTT AGAAAAGCGG GCGTTTTAA	999
15	·	
	(2) INFORMATION FOR SEQ ID NO:55:	
•	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 816 base pairs	
20	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
25		
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
20		
30	(vi) ORIGINAL SOURCE:	•
30	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
30	(A) ORGANISM: Helicobacter pylori	
30	(A) ORGANISM: Helicobacter pylori (ix) FEATURE:	
	(A) ORGANISM: Helicobacter pylori(ix) FEATURE:(A) NAME/KEY: misc_feature	
30	(A) ORGANISM: Helicobacter pylori (ix) FEATURE:	
	(A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1816	
	(A) ORGANISM: Helicobacter pylori(ix) FEATURE:(A) NAME/KEY: misc_feature	
	(A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1816 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:	
35	(A) ORGANISM: Helicobacter pylori (ix) FEATURE:	60
	(A) ORGANISM: Helicobacter pylori (ix) FEATURE:	120
35	(A) ORGANISM: Helicobacter pylori (ix) FEATURE:	120 180
35	(A) ORGANISM: Helicobacter pylori (ix) FEATURE:	120 180 240
35	(A) ORGANISM: Helicobacter pylori (ix) FEATURE:	120 180 240 300
35	(A) ORGANISM: Helicobacter pylori (ix) FEATURE:	120 180 240 300 360
35	(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1816 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55: ATGAACATAT TCAAGCGTAT TATTTGCGTA ACCGCTATTG TTTTAGGTTT TTTTAACCTT TTAGACGCCA AACACCACAA AGAAAAAAAA GAAGACCACA AAATCACTCG TGAGCTTAAA GTGGGCGCTA ACCCTGTGCC GCATGCGCAA ATCTTGCAAT CAGTTGTGGA TGATTTGAAA GAGAAAGGGA TCAAATTAGT GATCGTGTCT TTTACGGATT ATGTGTTGCC TAATTTAGCG CTCAATGACG GCTCTTTAGA CGCGAATTAC TTCCAGCACC GCCCTTATTT GGATCGGTTT AATTTGGACA GAAAAATCAC AGACATTAAA AACCTTAAAA AAGGCTCAGT GATTGCTGTG	120 180 240 300 360 420
35	(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1816 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55: ATGAACATAT TCAAGCGTAT TATTTGCGTA ACCGCTATTG TTTTAGGTTT TTTTAACCTT TTAGACGCCA AACACCACAA AGAAAAAAAA GAAGACCACA AAATCACTCG TGAGCTTAAA GTGGGCGCTA ACCCTGTGCC GCATGCGCAA ATCTTGCAAT CAGTTGTGGA TGATTTGAAA GAGAAAGGGA TCAAATTAGT GATCGTGTCT TTTACGGATT ATGTGTTGCC TAATTTAGCG CTCAATGACG GCTCTTTAGA CGCGAATTAC TTCCAGCACC GCCCTTATTT GGATCGGTTT AATTTGGACA GAAAAATGAA CCTTGTTGGT TTGCCCAATA TCCATGTGGA GCCTTTAAGA TTTTATTCTC AAAAAATCAC AGACATTAAA AACCTTAAAA AAGGCTCAGT GATTGCTGTG CCCAAATGATC CGGCCAATCA AGGCCTTATC	120 180 240 300 360 420 480
35	(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1816 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55: ATGAACATAT TCAAGCGTAT TATTTGCGTA ACCGCTATTG TTTTAGGTTT TTTTAACCTT TTAGACGCCA AACACCACAA AGAAAAAAAA GAAGACCACA AAATCACTCG TGAGCTTAAA GTGGGCGCTA ACCCTGTGCC GCATGCGCAA ATCTTGCAAT CAGTTGTGGA TGATTTGAAA GAGAAAGGGA TCAAATTAGT GATCGTGTCT TTTACGGATT ATGTGTTGCC TAATTTAGCG CTCAATGACG GCTCTTTAGA CGCGAATTAC TTCCAGCACC GCCCTTATTT GGATCGGTTT AATTTGGACA GAAAAATGAA CCTTGTTGGT TTGCCCAATA TCCATGTGGA GCCTTTAAGA TTTTATTCTC AAAAAATCAC AGACCATAAA AACCTTAAAA AAGGCTCAGT GATTGCTGTG CCAAATGATC CGGCCAATCA AGGCCTTATC GCCCAATGACC AGCCCAATCA ACCCCAAGCAA TCTATACGCT ACGGAGTTTG ATATTGTCAA AAATCCTTAC	120 180 240 300 360 420 480 540
35	(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1816 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55: ATGAACATAT TCAAGCGTAT TATTTGCGTA ACCGCTATTG TTTTAGGTTT TTTTAACCTT TTAGACGCCA AACACCACAA AGAAAAAAAA GAAGACCACA AAATCACTCG TGAGCTTAAA GTGGGCGCTA ACCCTGTGCC GCATGCGCAA ATCTTGCAAT CAGTTGTGGA TGATTTGAAA GAGAAAGGGA TCAAATTAGT GATCGTGTCT TTTACGGATT ATGTGTTGCC TAATTTAGCG CTCAATGACG GCTCTTTAGA CGCGAATTAC TTCCAGCACC GCCCTTATTT GGATCGGTTT AATTTGGACA GAAAAATGAC CCTTGTTGGT TTGCCCAATA TCCATGTGGA GCCTTTAAGA TTTTATTCTC AAAAAATCAC AGACCATAAA AACCTTAAAA AAGGCTCAGT GATTGCTGTG CCAAATGATC CGGCCAATCA AGGCAGGGCG TTGATTTTAC TCCATAAACA AGGCCTTATC GCTCTCAAAG ACCCCAAGCAA TCTATACGCT ACGGAGTTTG ATATTGTCAA AAATCCTTAC AACATCAAAA TCAAACCCCT AGAAGCTGCG TTATTGCCTA AGGTTTTTAGG GGATGTGGAT	120 180 240 300 360 420 480 540 600
35	(A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1816 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55: ATGAACATAT TCAAGCGTAT TATTTGCGTA ACCGCTATTG TTTTAGGTTT TTTTAACCTT TTAGACGCCA AACACCACAA AGAAAAAAAA GAAGACCACA AAATCACTCG TGAGCTTAAA GTGGGCGCTA ACCCTGTGCC GCATGCGCAA ATCTTGCAAT CAGTTGTGGA TGATTTGAAA GAGAAAGGGA TCAAATTAGT GATCGTGTCT TTTACGGATT ATGTGTTGCC TAATTTAGCG CTCAATGACG GCTCTTTAGA CGCGAATTAC TTCCAGCACC GCCCTTATTT GGATCGGTTT AATTTGGACA GAAAAATGCA CCTTGTTGGT TTGGCCAATA TCCATGTGGA GCCTTTAAGA TTTTATTCTC AAAAAATCAC AGACATTAAA AACCTTAAAA AAGGCTCAGT GATTGCTGTG CCAAATGATC CGGCCAATCA AGGCAGGGCG TTGATTTTAC TCCATAAACA AGGCCTTATC GCTCTCAAAG ACCCAAGCAA TCTATACGCT ACGGAGTTTG ATATTGTCAA AAATCCTTAC AACATCAAAA TCAAACCCCT AGAAGCTGCG TTATTGCCTA AGGTTTTAGG GGATGTGGAT GGGGCTATCA TAACAGGGGAA TTATGCCTTG CAAGCAAAAC TCACCGGAGC CTTATTTTCA	120 180 240 300 360 420 480 540 600 660
35 40 45	(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1816 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55: ATGAACATAT TCAAGCGTAT TATTTGCGTA ACCGCTATTG TTTTAGGTTT TTTTAACCTT TTAGACGCCA AACACCACAA AGAAAAAAAA GAAGACCACA AAATCACTCG TGAGCTTAAA GTGGGCGCAA ACCCTGTGCC GCATGCGCAA ATCTTGCAAT CAGTTGTGGA TGATTTGAAA GAGAAAAGGGA TCAAATTAGT GATCGTGTCT TTTACGGATT ATGTGTTGCC TAATTTAGCG CTCAATGACG GCTCTTTAGA CGCGAATTAC TTCCAGCACC GCCCTTATTT GGATCGGTTT AATTTGGACA GAAAAATCAC ACCTTGTTGGT TTGGCCAATA TCCATGTGGA GCCTTTAAGA TTTTTATTCTC AAAAAATCAC AGACATTAAA AACCTTAAAA AAGGCTCAGT GATTGCTGTG CCAAATGATC CGGCCAATCA AGGCAGGGCG TTGATTTTAC TCCATAAACA AGGCCTTATC GCTCTCAAAG ACCCAAGCAA TCTATACGCT ACGGAGTTTG ATATTGTCAA AAATCCTTAC AACATCAAAA TCAAACCCCT AGAAGCTGCG TTATTTGCCTA AGGTTTTAGG GGATGTGGAT GGGGCTATCA TAACAGGGGAA TTATGCCTTG CAAGCAAAAC TCACCGGAGC CTTATTTTCA GAAGATTAAAG ACTCGCCTTA TGCTAATCTT GTAGCCTCTC GTGAGGATAA TGCGCCAAGAT	120 180 240 300 360 420 480 540 600 660 720
35 40 45	(A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1816 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55: ATGAACATAT TCAAGCGTAT TATTTGCGTA ACCGCTATTG TTTTAGGTTT TTTTAACCTT TTAGACGCCA AACACCACAA AGAAAAAAAA GAAGACCACA AAATCACTCG TGAGCTTAAA GTGGGCGCTA ACCCTGTGCC GCATGCGCAA ATCTTGCAAT CAGTTGTGGA TGATTTGAAA GAGAAAGGGA TCAAATTAGT GATCGTGTCT TTTACGGATT ATGTGTTGCC TAATTTAGCG CTCAATGACG GCTCTTTAGA CGCGAATTAC TTCCAGCACC GCCCTTATTT GGATCGGTTT AATTTGGACA GAAAAATGCA CCTTGTTGGT TTGGCCAATA TCCATGTGGA GCCTTTAAGA TTTTATTCTC AAAAAATCAC AGACATTAAA AACCTTAAAA AAGGCTCAGT GATTGCTGTG CCAAATGATC CGGCCAATCA AGGCAGGGCG TTGATTTTAC TCCATAAACA AGGCCTTATC GCTCTCAAAG ACCCAAGCAA TCTATACGCT ACGGAGTTTG ATATTGTCAA AAATCCTTAC AACATCAAAA TCAAACCCCT AGAAGCTGCG TTATTGCCTA AGGTTTTAGG GGATGTGGAT GGGGCTATCA TAACAGGGGAA TTATGCCTTG CAAGCAAAAC TCACCGGAGC CTTATTTTCA	120 180 240 300 360 420 480 540 600 660

```
(i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 951 base pairs
                (B) TYPE: nucleic acid
                (C) STRANDEDNESS: double
               (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
         (iii) HYPOTHETICAL: NO
10
         (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
15
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
               (B) LOCATION 1...951
20
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:
     ATGCAAGAAT TCAGTTTGTG GTGCGATTTT ATAGAAAGGG ATTTTTTAGA AAACGATTTT
     TTAAAGCTCA TCAATAAGGG GGCTATTTGC GGGGCGACGA GTAACCCTAG TTTGTTTTGC
     GAAGCGATCA CAAAAAGCGC GTTTTATCAA GATGAAATCG CTAAACTCAA AGGCAAAAAA
     GCTAAAGAAA TTTATGAAAC TCTGGCACTA AAGGATATTT TACAAGCCTC TAGCGCGTTA
     ATGCCTTTGT ATGAAAAAGA CCCTAACAAC GGCTACATCA GCCTAGAAAT TGACCCCTTT
     TTAGAAGACG ATGCGATTAA AAGCATTGAT GAAGCCAAGC GGTTATTCAA AACATTAAAC
     CGCCCCAATG TGATGATTAA AGTCCCGGCG AGTGAAAGCG CTTTTGAAGT CATTAGCGCT
     CTGGCTCAAG CCTCTATCCC CATTAATGTA ACTTTAGTCT TTTCGCCTAA AATTGCCGGT
     GAAATCGCTC AAATCTTAGC CAAAGAAGCA CGAAAAAGAG CGGTCATTAG CGTGTTTGTC
     TCACGATTTG ACAAAGAAAT AGACCCACTA GTGCCACAAA ATTTGCAAGC TCAAAGTGGG 600
     ATCATGAACG CTACCGAGTG TTATTATCAA ATCAACCAGC ATGCTAATAA GCTAATAAGC
     ACCCTTTTTG CATCCACCGG CGTTAAATCT AATTCTTTAG CTAAAGATTA CTACATTAAA
     GCGCTGTGTT TTAAAAACTC TATCAACACA GCCCCCTAG ACGCCCTAAA CGCTTATTTG
                                                                         780
35
     CTTGACCCAA ACACCGAGTG TCAAACCCCT TTAAAAATCA CAGAAATTGA AGCGTTCAAA
                                                                         840
     AAAGAATTAA AAACGCACAA TATTGATTTA GAAAACACCG CCCAAAAACT CCTTAAAGAA
                                                                         900
     GGCTTGATAG CGTTCAAACA ATCCTTTGAA AAGCTTTTAA GCAGTTTTTG A
                                                                         951
     (2) INFORMATION FOR SEQ ID NO:57:
40
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 783 base pairs
               (B) TYPE: nucleic acid
               (C) STRANDEDNESS: double
45
               (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
        (iii) HYPOTHETICAL: NO
50
         (iv) ANTI-SENSE: NO
```

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

600

660

55

•	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1783</pre>	
5	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:	
٠	(AI) BEQUERCE BESCRIFTION. BEQ IS NO.51.	
	ATGAAAACAA ATGGTCATTT TAAGGATTTT GCATGGAAAA AATGCTTTTT AGGCGCGAGC	60
	GTGGTGGCTT TATTAGTGGG GTGTAGCCCG CATATTATTG AAACCAATGA AGTTGCTTTG	120
	AAATTGAATT ACCATCCAGC TAGCGAGAAA GTTCAAGCGT TAGATGAAAA GATTTTACTT	180
10	TTAAGGCCAG CTTTCCAATA CAGCGATAAT ATTGCTAAAG AGTATGAAAA CAAATTCAAG	240
	AATCAAACCA CGCTTAAAGT TGAAGAGATC TTGCAAAATC AGGGCTATAA GGTTATTAAT	300
	GTGGATAGCA GCGATAAAGA CGATTTTTCT TTTGCGCAAA AAAAAGAAGG GTATTTGGCT	360
	GTCGCTATGA ATGGCGAAAT TGTTTTACGC CCCGATCCTA AAAGGACCAT ACAGAAAAAA	420
	TCAGAACCCG GGTTATTATT CTCCACTGGT TTGGATAAAA TGGAAAGGGT TTTAATCCCG	480
15	GCTGGGTTTG TCAAGGTTAC CATACTAGAG CCTATGAGTG GGGAATCTTT GGATTCTTTT	540
	ACGATGGATT TGAGCGAGTT GGACATCCAA GAAAAATTCT TAAAAACCAC CCATTCAAGC	600
	CATAGCGGAG GGTTAGTTAG CACTATGGTT AAGGGGACGG ATAATTCTAA TGACGCAATT	660
	AAGAGCGCTT TGAATAAGAT TTTTGCAAGT ATCATGCAAG AAATGGATAA GAAACTCACT	720
20	CAAAGGAATT TAGAATCTTA TCAAAAAGAC GCCAAGGAAT TAAAAAAACAA GAGAAACCGA	780 783
20	TAA	703
	(2) INFORMATION FOR SEQ ID NO:58:	
	() another draps of the control of	
25	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 4149 base pairs	
23	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
30	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	•
	(iv) ANTI-SENSE: NO	
35	(24) 1812 521521 110	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	
40	(A) NAME/KEY: misc_feature	
	(B) LOCATION 14149	
•		
•	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:	
45	TTGAATTTTA ATAACCTTAC GGCTAATGGG GCGTTAAATT TTAATGGTTA TGCGCCCTCT	60
73	TTAACTAAGG CTTTAATGAA TGTCAGCGGG CAGTTTGTTT TAGGGAATAA TGGGGATATT	120
	AATTTATCTG ACATCAATAT CTTTGACAAC ATCACAAAAT CTGTAACTTA CAACATCTTA	180
	AACGCTCAAA AAGGGATTAC TGGCATTAGT GGGGCTAATG GCTATGAAAA AATCCTTTTT	240
	TATGGCATGA AAATCCAAAA CGCTACCTAT AGCGATAATA ACAACATCCA AACTTGGTCG	300
50	TTTATAAACC CTCTCAATTC TTCTCAAATC ATTCAAGAGA GCATTAAAAA TGGGGATCTA	360
	ACCATAGAAG TITTAAATAA CCCTAACTCG GCTTCCAACA CTATTTTAA TATCGCTCCT	420

GAGCTTTATA ATTACCAAGA TTCTAAGCAA AATCCTACCG GCTATAGCTA TGATTATAGC GACAATCAAG CAGGCACTTA TTACTTGACA AGCAACATTA AAGGTCTTTT CACCCCTAAA

GGCTCTCAAA CGCCTCAAAC CCCAGGCACT TATAGCCCAT TTAACCAGCC TTTGAATAGT

TTGAATATCT ACAATAAGGG TTTTTCTAGC GAGAATTTAA AAACGCTTTT AGGGATCCTT

					•		
•	TCTCAAAATT	CCGCCACCTT	AAAAGAAATG	ATTGAATCCA	ACCAACTAGA	CAATATCACT	720
	AACATTAATG	AAGTGTTGCA	ACTCTTAGAT	AAGATTAAAA	TCACCCAAGO	GCAAAAGCAA	780
	GCGCTCCTAG	AAACGATCAA	CCATTTGACT	GACAACATCA	ATCAAACCTT	TAATAACGGG	840
	AATCTCGTTA	TAGGCGCTAC	CCAAGATAAT	GTTACAAACT	CTACTAGCTC	TATATGGTTT	900
5	GGGGGCAATG	GCTATAGCAG	CCCTTGCGCG	CTAGATAGCG	CCACTTGTTC	TTCTTTTAGA	960
	AACACTTACT	TGGGGCAATT	ATTAGGCTCA	ACTTCCCCTT	ATTTAGGCTA	CATTAACGCT	1020
	GATTTTAAAG	CTAAAAGCAT	TTATATTACC	GGGACAATTG	GAAGTAGTAA	CGCTTTTGAA	1080
	AGCGGAGGGA	GCGCGGATGT	AACCTTTCAA	AGCGCTAATA	ACTTAGTGTT	GAATAAAGCT	1140
	AACATAGAAG	CTCAAGCCAC	AGACAATATC	TTTAATCTTT	TGGGTCAAGA	AGGGATTGAT	1200
10	AAAATCTTTA	ATCAGGGGAA	TTTAGCGAAT	GTTCTTAGTC	AAATGGCTAT	GGAAAAAATC	1260
	AAGCAAGCCG	GCGGTTTAGG	GAACTTTATA	GAAAACGCTC	TAAGCCCTTT	GAGTAAGGAA	1320
• .	TTACCCGCTA	GCTTGCAAGA	TGAAACCTTA	GGCCAACTTA	TAGGTCAAAA	TAACTTAGAT	1380
	GATTTATTGA	ATAATAGTGG	AGTCATGAAT	GAAATCCAAA	ACATTATCAG	TCAAAAACTA	1440
	AGCATTTTTG	GCAATTTTGT	TACCCCATCC	ATCATAGAAA	ACTACCTTGC	TAAGCAGTCT	1500
15	TTAAAAAGCA	TGCTAGACGA	TAAAGGGCTT	TTGAATTTTA	TCGGTGGGTA	TATAGACGCT	1560
	TCTGAATTAA	GCTCTATTTT	AGGCGTGATT	TTAAAGGATA	TTACTAACCC	CCCTACAAGC	1620
	CTGCAAAAAG	ACATTGGTGT	GGTAGCGAAC	GACTTGTTGA	ACGAGTTTTT	AGGACAAGAT	1680
	GTTGTCAAAA	AGCTAGAAAG	TCAAGGCTTG	GTGAGTAATA	TCATCAATAA	TGTTATTTCT	1740
	CAAGGCGGGT	TGAGCGGCGT	TTATAATCAA	GGTTTAGGGA	GCGTGTTGCC	GCCCTCTTT	1800
20	CAAAACGCGC	TCAAAGAAAA	CGATTTAGGC	ACTCTTTTAT	CGCCTAGAGG	CTTGCATGAT	1860
	TTTTGGCAAA	AAGGGTATTT	TAACTTTTTA	AGCAATGGCT	ATGTTTTTGT	CAATAACAGC	1920
	TCTTTTAGTA	ACGCTACTGG	GGGTAGTTTG	AATTTTGTCG	CCAACAAGTC	TATIMENCAGE	1980
	AATGGCGATA	ATACGATTGA	CTTTAGCAAG	TATCAAGGCG	CATTGATTT	TCCTTCTNAT	2040
	GGTGTTTCTA	ATATCAATAT	CACCACCCTA	AACGCCACTA	ATGGCTTAAG	ССТТААТССС	2100
25	GGTTTGAATA	ATGTGAGCGT	TCAAAAAGGA	GAAATTTGTA	TCAATTTAGC	CAATTGCCCT	2160
	ACAACCAAAA	ACAGCTCTCC	TGCAAACTCT	AGCGTAACCC	CCACTAATGA	GTCTTTAACC	2220
	GTGCACGCTA	ATAATTTCAC	TTTCTTAGGC	ACAATCATCT	CTAATGGGGC	TATTCATTC	2280
	TCTCAAGTAA	CAAATAATAG	CGTTATAGGC	ACGCTCAATC	TCAATGAAAA	TGCGACCTTG	2340
	CAAGCTAATA	ATTTAACGAT	CACCAACGCT	TTTAACAACG	CCTCTAACTC	TACGGCTAAT	2400
30	ATTGATGGTA	ATTTCACCTT	AAACCAACAA	GCGACTTTAA	GCACTAACGC	TAGTGGTTTG	2460
	AATGTCATGG	GGAATTTTAA	TAGCTATGGC	GATTTGGTGT	TTAACCTCAG	TCATTCACTT	2520
	AGTCATGCTA	TTATCAATAC	TCAAGGCACA	GCGACGATCA	TGGCCAATAA	TAACCCTTTC	2580
	ATCCAATTCA	ACGCTTCTTC	AAAAGAAGTG	GGTACTTACA	CGCTGATTGA	TAGCGCTAAA	2640
	GCCATTTATT	ACGGGTATAA	CAACCAAATC	ACAGGAGGCA	GTAGCCTGGA	TAATTACCTT	2700
35	AAGCTTTATG	CGCTCATTGA	TATTAATGGC	AAGCACATGG	TGATGACTGA	CAACGGCTTA	2760
	ACCTATAACG	GGCAAGCCGT	GAGCGTTAAA	GATGGCGGTT	TAGTTGTAGG	CTTTAACCAC	2820
	TCTCAAAATC	AATACATTTA	CACTTCCATT	CTTTATAATA	AAGTGAAAAT	CCCTCTTTCT	2880
	AATGATCCTA	TCAATAACCC	ACAAGCCCCC	ACTTTAAAAC	AATATATCCC	TCADATTCAG	2940
	GGCGTTCAAA	GCGTGGATAG	CATCGATCAA	GCTGGGGGAA	ATCANGCGAT	TAATTGGCTC	3000
40	AATAAAATCT	TTGAAACTAA	AGGAAGCCCT	TTATTCGCTC	CCTATTATCT	AGAGAGCCAC	3060
	TCCACAAAAG	ATTTAACCAC	GATCGCTGGA	GATATTGCTA	ACACTTTAGA	ACTCATCCCT	3120
	AACCCTAATT	TTAAAAATGA	CGCCACTAAT	ATTTTACAGA	TCAACACCTA	CACGCAGCAA	3120
•	ATGAGTCGTT	TAGCCAAGCT	CTCTGACACT	TCAACTTTCG	CCCGTTCTCA	TTTCTTAGAA	3240
	CGCTTAGAAG	CCCTTAAAAA	CAAGCGATTC	GCTGATGCGA	TCCCTAACGC	TATECATETE	
45	ATTTTAAAAT	ACTCTCAAAG	GAATAGAGTT	AAAAATAATG	TCTCCCCCAC	AGGAGTTGGA	3300 3360
•	GGGGCTAGTT	TCATTAGTGG	AGGTACTGGA	ACTTTATATC	GTATCA ATGT	AGGAGIIGGA	3420
	AGGTTTATTA	AGGGCGTGAT	TGTGGGAGGT	TATGCCGCTT	ATGGGTATAG	CCCCTTCCAT	
	GCAAACATCA	CTCAATCAGG	CTCTAGCAAT	GTCAATGTGG	CCCTTTTATA	CCCACCCONT	3480
	ATCAAAAGAA	GCGAGCTAAC	CATGAGCTTG	AATGAGAGT	GCGTTIMIAG	TA A A COMMO	3540
50	ATCAACTCCT	ATGACCCCCT	ACTCTCAATC	ATCAATCACT	CTTACACATA	COLCACACTTTC	3600
•	ACGACTGACG	CTAAAATCAA	TTATGGCTAT	CVALALAC VACA	TTALAGATA	AACCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	3660
	TTTAAACCCC	AAGTAGGCTT	AAGCTATTAT	TACATOL	TOTOTOTOTO	AAGCGTTATT	3720
	ATGGATGATC	CTATTTACAA	CCAATTCACA	CCCDAMCCMC	ACCOMPANY.	AAGGGGCATT	3780
	CTAACGATCA	ATTTTGCCCT	AGAAAGTCCC	CVALIBRIA	ACCUTAATAA	AAAATCCGTT	3840
55	GTGATTGCGG	ATGTGGGCAG	AGACTTRATTCGG	ATTAITICA.	ATAAAAACTC	TTATTATTTT	3900
				ALLMALICTA	1 GGGGATAA	AATGGTGCGT	3960

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TTCATCGGTA ATAACACCCT AAGCTATAGA GATGGTGGCA ATTATCACAG GCGGGGAGAT AAGATTGTTC AAAACCTTTT GCTAGGTTTG GGCTTGATTA TAAAGATATT AATATTACCG GCTTTTTAA	ATGTGAATGC	GGGCATAGGG	4020 4080 4140 4149
(2) INFORMATION FOR SEQ ID NO:59:			
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 789 base pairs (B) TYPE: nucleic acid			
(C) STRANDEDNESS: double (D) TOPOLOGY: circular			
(ii) MOLECULE TYPE: DNA (genomic)			
(iii) HYPOTHETICAL: NO			
(iv) ANTI-SENSE: NO			٠
<pre>(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori</pre>			
<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1789</pre>			
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(2) INFORMATION FOR SEQ ID NO:60:			
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 741 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular (ii) MOLECULE TYPE: DNA (genomic)			

(iii) HYPOTHETICAL: NO

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	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
5	(1)	
	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
:	(B) LOCATION 1741	
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:	
	ATGAAACAAT TTAAAAAGAA ACCAAAAAAG ATAAAACGAT CGCATCAAAA TCAAAAAACA	60
	ATCTTAAAGC GTCCTTTATG GCTTATGCCT TTACTGATTG GCGGGTTTGC TAGTGGGGTG	120
	TATGCGGATG GAACAGACAT TTTGGGGCTT AGTTGGGGGG AAAAAAGCCA AAAGGTATGC	180
15	GTGCATCGTC CATGGTATGC TATATGGAGT TGCGATAAAT GGGAGGAAAA AACACAACAA	240
	TTTACAGGAA ACCAACTCAT CACAAAAACT TGGGCAGGGG GTAATGCGGC TAACTACTAC	300
	CACTCTCAAA ACAACCAAGA CATCACAGCC AATTTAAAAA ATGATAACGG CACTTATTTT	360
•	TTAAGCGGTC TGTATAACTA CACCGGAGGG GAATATAATG GGGGGAATTT AGACATTGAA	420
•	TTAGGCAGTA ACGCTACTTT TAATCTAGGT GCGAGTAGTG GGAATAGCTT CACTTCTTGG	480
20	TATCCTAATG GGCATACTGA TGTTACTTTT AGCGCTGGGA CTATCAATGT GAATAACAGC	540
	GTAGAAGTGG GCAATCGTGT GGGATCGGGA GCTGGCACGC ACACCGGCAC AGCCACTTTA	600
	AACTTGAACG CTAATAAGGT TACTATCAAT TCCAATATCA GCGCGTATAA AACTTCGCAA	660
	GTGAATGTAG GCAATGCTAA CAGCGTTATT ACCATTAATT CGGTTTCTTT AAATGGGGAA	720
25	TACTTGCAGT TCTTTAGCTA G	741
23	(2) INFORMATION FOR SEQ ID NO:61:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 738 base pairs	
30	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
35	(II) MODECODE IIFE. DAN (GENOMIC)	
55	(iii) HYPOTHETICAL: NO	
-	(iv) ANTI-SENSE: NO	
		-
40	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
•	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
45	(B) LOCATION 1738	
	(with appropriate programmer) and the world	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:	•
	ATGATAAAAA AGACCCTTGC ATCGGTTTTA TTAGGATTGA GTTTGATGAG TGTGTTAAAT	60
50	GCCAAAGAAT GCGTTTCGCC CATAACAAGA AGCGTTAAGT ATCATCAGCA AAGTGCTGAG	120
	ATCAGAGCCT TGCAATTACA AAGTTACAAA ATGGCGAAAA TGGCGCTAGA CAATAACCTT	180
	AAGCTCGTTA AAGACAAAAA GCCAGCCGTC ATCTTGGATT TAGATGAAAC CGTTTTGAAC	240
	ACTITIGATI ATGCGGGCTA TITAGTCAAA AACTGCATTA AATACACCCC AGAAACTIGG	300
	GATAAATTTG AAAAAGAAGG CTCTCTTACG CTCATTCCTG GAGCGCTAGA CTTTTTAGAA	360
55	TACGCTAATT CTAAGGGCGT TAAGATTTTT TACATTTCTA ACCGCACCCA AAAAAATAAG	420

	TTGTTAAAGG AAAAAGGCAA GCCTAAAGCC GTTAGGCGGG AGTTAGTCGC TAAGGATTAT GCGATTGTTT TACAAGTGGG CGACACTTTG CATGATTTTG ACGCCATTTT TGCTAAAGAC	540 600
5	GCTAAAAACA GCCAAGAACA ACAAGCCAAA GTCTTGCAAA ACGCTCAAAA ATTCGGCACA GAATGGATCA TTTTACCCAA CTCTCTTTAT GGCACATGGG AAGATGGGCC TATAAAAGCA TGGCAAAATA AAAAATAA	660 720 738
	(2) INFORMATION FOR SEQ ID NO:62:	
10	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 867 base pairs(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
15	(b) TOPOLOGY: CIrcular	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
20	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
25	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1867</pre>	
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:	
	TTGTGGTGTT TAAAAACCCC TATCATAGGG CATGGCATGA AGAAAAAAGC AAAAGTCTTT	60
	TGGTGTTGTT TTAAAATGAT TCGTTGGTTG TATTTGGCGG TCTTTTTTTT GTTGAGCGTA TCAGACGCTA AAGAAATCGC TATGCAACGA TTTGACAAAC AAAACCATAA GATTTTTGAA	120
	ATCCTTGCGG ATAAAGTGAG CGCCAAAGAC AATGTGATAA CCGCCTCAGG GAATGCGATC	180 240
35	CTATTGAATT ATGACGTGTA TATTCTAGCG GATAAGGTGC GTTATGACAC CAAGACTAAA	300
	GAAGCGTTAT TAGAAGGCAA TATTAAGGTT TATAGGGGCG AGGGCTTGCT CGTTAAAACC	360
	GATTATGTGA AATTGAGTTT GAACGAAAAA TATGAGATCA TTTTCCCCTT TTATGTCCAA	420
	GACAGCGTGA GCGGGATTTG GGTGAGCGCG GATATTGCTA GCGGGAAGGA TCAAAAATAT	
40	AAGATTAAAA ACATGAGCGC TTCAGGGTGC AGCATTGACA ACCCCATTTG GCATGTCAAT GCGACTTCAG GCTCATTTAA CATGCAAAAA TCGCATTTGT CAATGTGGAA TCCTAAGATT	540
	TATGTCGGCG ATATTCCTGT ATTGTATTTG CCCTATATTT TCATGTCCAC GAGCAATAAA	600 660
	AGAACTACCG GGTTTTTATA CCCTGAGTTT GGCACTTCCA ACTTAGACGG CTTTATTTAT	720
	TTGCAACCCT TTTATTTAGC CCCCAAAAAC TCATGGGATA TGACCTTTAC CCCACAAATC	780
	CGTTACAAAA GGGGTTTTGG CTTGAATTTT GAAGCGCGCT ACATCAACTC TAAGACGCAG	840
45	GTTTTTATTC AATGCGCGCT ATTTTAG	867
	(2) INFORMATION FOR SEQ ID NO:63:	•
	(i) SEQUENCE CHARACTERISTICS:	
50	(A) LENGTH: 387 base pairs	
	(B) TYPE: nucleic acid	*
	(C) STRANDEDNESS: double	

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: DNA (genomic)

```
(iii) HYPOTHETICAL: NO
          (iv) ANTI-SENSE: NO
 5
          (vi) ORIGINAL SOURCE:
                (A) ORGANISM: Helicobacter pylori
          (ix) FEATURE:
10
                (A) NAME/KEY: misc_feature
                (B) LOCATION 1...387
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:
15
     TTGATGTTTA AAAAAATGTG TTTGAGCCTG CTAATGATAA GCGGTGTTTG TGTGGGGGCA
                                                                           60
     AAGGATTTGG ATTTCAAGCT GGATTATCGC GCGACTGGGG GGAAATTCAT GGGGAAAATG
                                                                          120
     ACGGACTCTA GTCTTTTAAG TATCACTTCT ATGAACGATG AACCGGTGGT GATTAAAAAC
     CTTATTGTCA ATAGGGGAAA TTCATGCGAA GCGACTAAAA AAGTAGAACC CAAATTTGGC
     GATAAGTTTA AAAAAGAAAA ACTCTTTGAT CATGAATTAA AATACTCGCA ACAGATATTT
                                                                          300
     TACCGCCTGG ATTGCAAGCC TAACCAATTG TTAGAAGTTA AAATCATCAC GGACAAGGGC
                                                                          360
     GAATATTACC ATAAATTTTC CAAATAG
                                                                          387
      (2) INFORMATION FOR SEQ ID NO:64:
25
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 510 base pairs
               (B) TYPE: nucleic acid
               (C) STRANDEDNESS: double
               (D) TOPOLOGY: circular
30
         (ii) MOLECULE TYPE: DNA (genomic)
        (iii) HYPOTHETICAL: NO
35
         (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
40
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
               (B) LOCATION 1...510
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:
45
     ATGCAAGCGT TAAAATCATT GCTTGAAGTG ATTACAAAAC TCCAGAATCT AGGCGGCTAT
    TTGATGCATA TAGCTATTTT CATCATTTTT ATTTGGATTG GAGGGCTTAA GTTTGTGCCT
     TACGAAGCTG AAGGGATCGC CCCTTTTGTG GCCAACTCCC CTTTCTTTC TTTCATGTAT
                                                                         180
    AAATTTGAAA AACCTGCATA CAAACAACAC AAAATGTCTG AATCCCAATC CATGCAAGAA
                                                                         240
    GAAATGCAAG ATAACCCTAA AATCGTTGAA AACAAAGAAT GGCATAAAGA AAACCGCACT
                                                                         300
    TATTTAGTGG CTGAAGGTTT AGGGATTACG ATCATGATCC TAGGCATTTT GGTGCTTTTG
                                                                         360
    GGGCTTTGGA TGCCTTTAAT GGGCGTAGTT GGGGGCTTGC TTGTCGCTGG AATGACGATC
    ACCACCCTAT TCTTTTTAT TCACAACGCC AGAAGTGTTT GTCAATCAGC ATTTCCCATG
                                                                         480
    GCTTTCTGGG GCTGGAAGGC TAGTGGTTAA
                                                                         510
55
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- 137 -

(2) INFORMATION FOR SEQ ID NO:65:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1464 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: circular
- (ii) MOLECULE TYPE: DNA (genomic)

10 (iii) HYPOTHETICAL: NO

- (iv) ANTI-SENSE: NO
- 15 (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Helicobacter pylori
 - (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
- 20 (B) LOCATION 1...1464
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

25 ATCGCTTTTA TTGCCGCCGG AATGATAGGT TGGGGGCAAT ACAGCTTTTC TTTAGATAGC GATAGCGCTG CCAAGATGGG ACAGATTAAG ATTTCTCAAG AAGAATTAGC CCAAGAATAC	120 180 240
CATACCCCTC CCAAGCTCGC ACAGATTAAC ATTTCTCAAC AACAATTACC CCAAGAATAC	
GNINGCOCIO CCARNOTOCO NCHOMITAGO MILICICANO MAGMITAGO CCANGANIAC	240
CGCCGCCTTA AAGACGCCTA TGCTGAGTCT ATCCCTGATT TTAAAGAACT CACCGAAGAT	240
CAAATCAAAG CCATGCATTT AGAAAAAAGC GCGCTAGATT CGCTCATCAA TCAAGCTTTA	300
TTGAGGAATT TCGCTTTAGA TTTAGGGCTT GGTGCTACCA AGCAAGAAGT GGCCAAAGAG	360
30 ATCAGAAAA CGAACGTTTT TCAAAAAGAT GGCGTTTTTG ATGAAGAATT GTATAAAAAT	420
ATCTTAAAAC AAAGCCATTA CCGCCCCAAG CATTTTGAAG AAAGCGTTGA AAGGCTTTTA	480
ATCCTTCAAA AAATCAGCGC TCTATTCCCC AAAACCACCA CCCCTTTGGA GCAATCCAGT	540
CTATCGCTTT GGGCAAAATT GCAAGACAAA TTAGACATTC TTATCCTAAA TCCTAATGAT	600
GTTAAAATCT CTCTCAATGA AGAAGAGATG AAAAAATATT ATGAAAACCA TAGAAAGGAT	660
35 TTTAAAAAGC CCACAAGCTT TAAAACACGC TCTTTATATT TTGACGCTAG TTTAGAAAAA	720
ACTGATTTGA AAGAGTTGGA GGAATACTAC CATAAAAACA AGGTGTCTTA TTTGGACAAA	780
GAGGGGAAAT TACAGGATTT TAAAAGCGTT CAAGAGCAAG TCAAGCATGA TTTAAACATG	840
CAAAAGGCGA ATGAAAAAGC CTTAAGGAGC TATATCGCTC TAAAAAAGGG GAACGCACAA	900
AACTACACCA CGCAAGATTT TGAAAAAAAC AACTCCCCCT ATACTGCTGA AATCACGCAA	960
40 AAACTCACCG CTCTCAAGCC CCTTGAAGTC CTAAAACCAG AGCCTTTTAA AGATGGTTTT	1020
ATCGTGGTGC AGCTTGTCTC TCAAATTAAA GACGAATTGC AAAATTTTGA TGAAGCCAAA	1080
AGCGCTCTTA AAACCCGTCT GACTCAAGAA AAAACCCTTA TGGCGTTGCA AACTTTAGCT	1140
AAAGAAAAGC TTAAGGATTT TAAAGGGAAA AGCGTGGGTT ATGTAAGCCC TAATTTTGGA	1200
GGCACTATCA GTGAACTTAA CCAAGAAGAG AGCGCGAAGT TTATCAACAC CCTTTTTAAC	1260
45 CGCCAGGAAA AAAAAGGGTT TGTAACCATA GGTAATAAAG TGGTGCTTTA TCAAATCACA	1320
GAGCAAAATT TCAATCACCC CTTTAGTGCA GAAGAAAACC AATACATGCA GCGTTTAGTC	1380
AATAACACTA AAACGGATTT TTTTGATAAA GCGTTGATAG AAGAATTGAA AAAACGCTAT	1440
AAGATAGTCA AATACATTCA ATAA	1464

- 50 (2) INFORMATION FOR SEQ ID NO:66:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 429 base pairs
 - (B) TYPE: nucleic acid
- 55 (C) STRANDEDNESS: double

	(b) TOPOLOGY: CIFCULAR	
	(ii) MOLECULE TYPE: DNA (genomic)	
5	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
10	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
15	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1429</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:	
20 25	ATGAAAACGA ACTTTTATAA AATTAAATTA CTATTTGCTT GGTGTCTTAT CATTGGCATG TTTAACGCTC CGCTTAACGC TGACCAAAAC ACGGATATAA AAGATATTAG TCCTGAAGAT ATGGCGCTAA ATAGCGTGGG GCTTGTTTCT AGAGATCAGC TAAAAATAGA GATCCCTAAA GAAACCCTAG AGCAAAAAGT GGCCATACTC AATGACTATA ATGATAAGAA TGTTAATATC AAGTTTGACG ACATAAGTTT AGGGAGTTTC CAACCTAATG ATAATCTAGG TATCAATGCG ATGTGGGGCA TTCAAAATCT TCTCATGAGC CAAATGATGA GCAATTACGG TCCAAACAAT TCTTTCATGT ATGGCTATGC GCCAACATAC TCAGATTCAT CGTTTTTACC ACCGATCTTA GGGTATTAA	60 120 180 240 300 360 420
23	(2) INFORMATION FOR SEQ ID NO:67:	429
30	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 627 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular	
35	(ii) MOLECULE TYPE: DNA (genomic)	
÷	(iii) HYPOTHETICAL: NO	
40	(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
45	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1627</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:	
50	TTGATCAACA ATAATAATAA CAATAAAAAA CTGAGAGGCT TTTTTTTGAA AGTTCTCTTA AGTCTCGTTG TTTTCAGTTC GTATGGGTCA GCAAATGACG ATAAAGAAGC CAAAAAAGAA GCGCTAGAAA AAGAAAAAAA CACTCCCAAT GGGCTTGTTT ATACGAATTT AGATTTTGAT AGTTTTAAAG CGACTATCAA AAATTTGAAA GACAAGAAAG TAACTTTCAA AGAAGTCAAT	120 180 240
55	CCCGATATTA TCAAAGATGA AGTTTTTGAC TTCGTGATTG TCAATAGAGT CCTTAAAAAA ATAAAGGATT TGAAGCATTA CGATCCAGTT ATTGAAAAAA TCTTTGATGA AAAGGGTAAA	300 360

5	GAAATGGGAT TGAATGTAGA ATTACAGATC AATCCTGAAG TGAAAGACTT TTTTACTTTC AAAAGCATCA GCACGACCAA CAAACAACGC TGCTTTCTAT CATTGCACGG AGAAACAAGA GAAATTTTAT GCGATGATAA GCTATATAAT GTTTTATTGG CCGTATTCAA TTCTTATGAT CCTAATGATC TTTTGAAACA CATTAGCACC ATAGAGTCTC TCAAAAAAAT CTTTTATACG ATTACATGTG AAGCGGTATA TCTATAA	420 480 540 600 627
10	(2) INFORMATION FOR SEQ ID NO:68: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 738 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular	
15	(ii) MOLECULE TYPE: DNA (genomic)	٠
20	(iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
25	<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1738 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:</pre>	
30	ATGACAGCAG CGATTATTCC TATTGTTGTG GGATTTACTA ATCCGCAAAT GACCGCTATC	60 120 180 240
35	ATCTTAAATA TCAGCAAATT AACAGGGGAA TTTAACGCGC AAGGCAACAC GCAAAGCGCG CAAATTAGTG CTGTCAATAG TCAGATTGCA AGCATTTTAG CGAGTAACAC TACCCCTAAA AATCCTAGCG CTATTGAAGC TTATGCGACG AATCAAATCG CTGTTCCTAG CGTGCCAACA ACGGTTGAAA TGATGAGCGG TATATTAGGC AATATTACAA GCGCAGCACC AAAATACGCC	300 360 420 480 540
40	CONTROL TO THE TOTAL CONTROL OF THE	
	GATTCCCTTG ATAGCTGTAC CGCTTTAGGC GCACTTGTTG GCTCATCAAA AGTGTTTTTC AGTTGCATGC AAATTTCTAT GACTCCTATG AGTGTTTCTA TGCCCACTGT TATGCCAAAT	600 660 720 738
45	GATTCCCTTG ATAGCTGTAC CGCTTTAGGC GCACTTGTTG GCTCATCAAA AGTGTTTTTC AGTTGCATGC AAATTTCTAT GACTCCTATG AGTGTTTCTA TGCCCACTGT TATGCCAAAT	660 720
• • •	GATTCCCTTG ATAGCTGTAC CGCTTTAGGC GCACTTGTTG GCTCATCAAA AGTGTTTTTC AGTTGCATGC AAATTTCTAT GACTCCTATG AGTGTTTCTA TGCCCACTGT TATGCCAAAT ACCAGCGGTT GCCACTAA	660 720
45	GATTCCCTTG ATAGCTGTAC CGCTTTAGGC GCACTTGTTG GCTCATCAAA AGTGTTTTTC AGTTGCATGC AAATTTCTAT GACTCCTATG AGTGTTTCTA TGCCCACTGT TATGCCAAAT ACCAGCGGTT GCCACTAA (2) INFORMATION FOR SEQ ID NO:69: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1104 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double	660 720

180

240

300

360

420

480

540

600

780

840

1080

1104

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(iv) ANTI-SENSE: NO
          (vi) ORIGINAL SOURCE:
                (A) ORGANISM: Helicobacter pylori
 5 -
          (ix) FEATURE:
                (A) NAME/KEY: misc_feature
                (B) LOCATION 1...1104
10
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:
     ATGATTAAAA GCGTAGAGAT TGAAAATTAC AAAAATTTTG AGCACCTTAA AATGGAAAAT
     TTTAAACTCA TCAACTTTTT TACCGGTCAA AACGATGCGG GTAAAACCAA TCTTTTAGAA
     GCTCTTTATA CCAACACAGG CCTTTGTGAT CCTACTGCCA ATCAAGTCAG TCTTCCTCCT
     GAACATGCCG TGAATATTAG TGAATTCAGA AAAATCAAAC TCGATGCCGA CAACCTAAAA
.15
     ACCTTTTTT ATCAAGGAAA CACCGCTAAT CCCATTAGTA TCCGCACTGA ATTTGAACAT
     GCTACTATCC CTCTTACTAT CCAATACCCC ACACAAACCA GTTACAGCAA AGACATCAAT
     TTGAATAGCG ATGATGCTCA TATGACAAAC CTTATAAACA CAACAATAAC GAAGCCACAG
     CTCCAATTTT CCTACAATCC ATCCCTTTCC CCCATGACAA TGACTTATGA ATTTGAAAGG
20
     CAAAACCTAG GTTTAATCCA TTCTAATTTA GATAAAATCG CTCAAACCTA TAAAGAAAAT
     GCGATGTTTA TTCCTATAGA ATTATCTATT GTTAATTCTC TTAAAGCATT GGAAAATTTA
     CAATTAGCAA GCAAAGAAAA AGAATTGATT GAAATCCTAC AATGTTTCAA CCCTAATATT
     TTAAATGCTA ATACAATAAG AAAGTCTGTC TATATCCAAA TCAAAGATGA AAACACACCG
     CTAGAAGAAA GTCCCAAAAG GCTTTTAAAT TTGTTTGGTT GGGGTTTTAT CAAATTCTTT
     ATTATGGTGA GCATTCTTAT AGACAATCGT GTCAAGTATC TTTTTATTGA TGAAATAGAA
     AGCGGTTTGC ACCATACAAA AATGCAAGAG TTTTTAAAAG CTCTGTTTAA GTTAGCTCAA
     AAATTACAGA TTCAAATTTT TGCCACCACG CACAATAAGG AATTTTTATT AAACGCCATC
     AACACGATAT CCGATAATGA AACGGGAGTT TTTAAAGACA TAGCCTTGTT TGAGCTTGAA 1020
     AAAGAAAGCG CTTCTGGCTT TATCAGACAC AGCTATTCTA TGCTAGAAAA AGCGCTTTAT
     AGGGGTATGG AGGTTAGAGG CTGA
     (2) INFORMATION FOR SEQ ID NO:70:
          (i) SEQUENCE CHARACTERISTICS:
35
               (A) LENGTH: 1230 base pairs
               (B) TYPE: nucleic acid
               (C) STRANDEDNESS: double
               (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
```

- 40
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Helicobacter pylori
- (ix) FEATURE: 50

- (A) NAME/KEY: misc_feature
 - (B) LOCATION 1...1230
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:
- ATGTCCTTGA TTAGAGTGAA TGGGGAAGCT TTTAAACTCT CTTTGGAAAG TTTAGAAGAA 55

660

	GATCCTTTTG AAACTAAAGA AACGCTAGAA ACGCTAGAAA CGCTTATCAA ACAAACGAGC	120
•	GTTGTTTTAT TGGCCGCTGG GGAGTCTAAG CGTTTTTCTC GTGCGATTAA AAAGCAGTGG	180
	CTACGCTCTC ACCACACCCC CTTATGGCTC AGCGTGTATG AAAGCTTTAA AGAAGCCCTA	240
	GACTTTAAGG AAGTCATTCT AGTTGTAAGC GAATTGGATT ATGTTTATAT CCAACGCCAT	300
5	TACCCCAAAA TCAAGCTTGT AAAAGGCGGG GCATCAAGGC AAGAATCCGT GCGTAACGCT	360
	TTGAAAGTAA TTGATAGCAC TTACACGATC ACCAGCGATG TGGCTAGGGG TTTAGCGAAT	420
	ATGGAAGCGC TTAAAAGCTT GTTTTTAACC CTCCAACAAA CGAGCCATTA TTGCATCGCC	480
	CCTTACTTGC CTTGCTATGA CACAGCGATC TATTATAACG AGGCTTTAGA TAGAGAAGCG	540
	ATCAAACTCA TTCAAACCCC GCAATTAAGC CACACCAAAA CGCTCCAATC AGCCCTAAAC	600
10	CAAGGGGGTT TTAAAGATGA AAGCAGCGCG ATTTTACAAG CTTTCCCTAA CTCTGTGAGC	660
	TATATTGAAG GCAGTAAGGA TTTGCACAAA CTCACCACAA GCGGCGATTT AAAGTTTTTT	720
	ACGCCTTTTT TTAACCCAGC AAAGGACACT TTTATAGGCA TGGGTTTTGA TACGCATGCG	780
	TTCATTAAAG ATAAGCCTAT GGTTTTAGGG GGGGTTGTTT TGGATTGCGA GTTTGGGTTA	840
	AAGGCTCATA GCGATGGCGA TGCTTTATTG CATGCGGTTA TTGATGCGAT TTTAGGAGCG	900
15	ATTAAAGGGG GGGATATTGG CGAATGGTTC CCTGATAATG ACCCCAAATA CAAAAACGCC	960
	TCTTCTAAAG AGCTTTTAAA AATCGTGTTG GATTTTCTC AAAGCATTGG GTTTGAATTG	1020
	CTTGAAATGG GAGCGACCAT CTTTAGCGAA ATCCCTAAAA TCACTCCTTA CAAACCGGCG	1080
	ATTTTAGAGA ATTTGAGCCA ACTTTTGGGT TTAGAAAAAT CTCAAATCAG CTTGAAAGCC	1140
	ACTACAATGG AAAAAATGGG GTTCATTGGC AAACAAGAAG GGCTGTTAGT CCAAGCGCAT	1200
20	GTGAGCATGC GTTATAAACA AAAACTTTAA	1230
	(2) INFORMATION FOR SEQ ID NO:71:	-
25	(i) SEQUENCE CHARACTERISTICS:	
25	(A) LENGTH: 813 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
30	(ii) MOLECULE TYPE: DNA (genomic)	
50	(II) HOLECOLE IIPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
	(111) milotimitans. No	
	(iv) ANTI-SENSE: NO	
35	(IV) ANII DENDE. NO	
<i>J J</i>	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
	(A) OKGANISM: NEITCODACCET pytori	
	(ix) FEATURE:	
40	(A) NAME/KEY: misc_feature	
	(B) LOCATION 1813	•
	(b) bockiton 1ol3	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:	
	10-1,,,,,,,,	
45	ATGAAAAGT TTGTAGCTTT AGGGCTTCTA TCCGCGGTTT TAAGCTCTTC GTTGTTAGCC	60
	GAAGGTGATG GTGTTTATAT AGGGACTAAT TATCAGCTTG GACAAGCCCG TTTGAATAGC	120
	AATATTTATA ATACAGGGA TTGCACAGGG AGTGTTGTAG GTTGCCCCCC AGGTCTTACC	180
	GCTAATAAGC ATAATCCAGG AGGCACCAAT ATCAATTGGC ACTCCAAATA CGCTAATGGG	240
	GCTTTGAATG GTTTTGGGTT GAATGTGGGT TATAAGAAAT TCTTCCAATT CAAGTCGCTA	300
50	GATATGACAA GCAAGTGGTT TGGTTTTAGA GTGTATGGGC TTTTTGATTA CGGGCATGCC	360
-	GATTTAGGTA AACAAGTTTA TGCACCTAAT AAAATCCAGT TGGATATGGT CTCTTGGGGT	420
	GTGGGGAGCG ATTTGTTAGC TGATATTATT GATAAAGACA ACGCTTCTTT TGGTATTTTT	480
	GGTGGGGTCG CTATCGGCGG TAACACTTGG AAAAGCTCTG CAGCAAACTA TTGGAAAGAG	540
	CAAATCATTG AAGCCAAAGG TCCTGATGTT TGTACCCCTA CTTATTGTAA CCCTAATGCC	600
55	COMPATAGO COACOME ALCOTOGO TOTO ACTOR COMPANDO DO CONTRA CA	660

CCTTATAGCA CCAACACTTC AACCGTCGCT TTTCAAGTGT GGTTGAATTT TGGGGTGAGA

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GCCAATATCT ACAAGCATAA TGGCGTGGAA TTTGGCGTGA (AAATTTTTGA GCGCGGGTCC TAACGCTACT AACCTTTATT T TCGCTTTATT TGGGGTATAA CTACACTTTT TAA	GAGTGCCGCT ACCATTTGAA	ACTCATCAAT ACGGGATTAT	720 780 813
(2) INFORMATION FOR SEQ ID NO:72:	•		
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1317 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular 			•
(ii) MOLECULE TYPE: DNA (genomic)		•	
(iii) HYPOTHETICAL: NO			
(iv) ANTI-SENSE: NO	•		
<pre>(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori</pre>			
<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 11317</pre>			
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:			
ATGGCTTACA AACCTAACAA AAAGAAGTTA AAAGAATTAA G AGCATCTTAG ATAAGGGCGA TGTTGCAACA AACAATCCTG T	GAGAGCAACC TTGAAGAGTC	GAATTTATTT	60 120
AATAAAATAC AAGAGCCACT CCCTTATGTC GTGAAAACGC A	AAATCAATAA	AGCAAGCATG	180
ATTTCTAGAG ATCCTATTGA ATGGGCAAAG TATTTAAGCT T	ITGAAAAACG .	AGTCTATAAG	240
GATAATAGTA AAGAAGATGT CAATTTCTTT GCCAATGGTG A	AGATAAAAGA .	AAGTTCTCGT	300
GTTTATGAAG CGAATAAAGA AGGGTTTGAA AGGCGCATCA C	TAAAAGATA	CGATCTGATT	360
GATAGAAATA TTGATAGAAA TAGAGAATTT TTTATAAAAG A ACAAACAGCT TAAAAGAATT GAAAGAGCAA GGGTTAGAAA T	AAATTGAAAT	TCTAACCCAC	420
GAAACGCATA AGAAAGCCTT AGAAAATGGC AATGAAATCG T	CCAATIGAC	CCACCATAAT	480
AAAGATATTT ACCAAGAAGT AGAAAGAACA AAAGATGGTG G	I I AAAGAATA Zammeemaae	CGACCATCTT	540 600
CCCAGTATTT CTAGCGCTGA GTATTTCAAG CTTTACAACA A	AACTGCCTTT	TGAAATAATC	660
AACAATGAAA ATACCAAACT GAATACTAAC GACAATGAAG A	AGTTAAAAA	ACTAGAATTT	720
GAATTAGCTA AAGAAGTGCA TATTTTAATC CTAGAGCAAC A	ATTGCTTTC	AGCAACAAAT	780
TATTATTCTT GGATAGATAA AGATGATAAT GCGAATTTTG C	TTGGAAAAT	GCATAGGCTT	840
ATCAATGAAA ATAAACTCAA AGAAAACCAT CTCAGCGCCA A	TAACGCTAA	TAAGATTAAG	900
CAATTTTCT TTAATAATGG TTCTATTTTA GGCTGGACTA A	AAGAAGAACA	AAGCGCTATA	960
CAAGAAAACA GAGATTATTC TTTAAGAAGC GCTCTTTTAA G	STTTAGAAGA	AATCGCTCAA	1020
GCAAAAATTG AATTGCAAAA ATACTATGAA AGCGTTTATG T	TAATGGTGA	IGGGAATAAA	1080
AGAGAAATCA AGCCTTTTAA AGAAATTTTA AGAGACACCA A	ACAATTTTGA	AAAAGCTTAT	1140
AAGGAGCGTT ATGACAAATT GGTAAGCTTG AGTGCAGCAA T GGTAATGAGC GACCAAATTC TAGTGCAAAT AACAATAACC C	CATTCAAGC '	I'AAAGAGGGT	1200
ACTAATACTT CTAACAATAT TATTCAAAAT AACAATAACC C	TATTAAAAA '	L'ACAATAGAG	1260
MIMINDER TO THE PROPERTY OF TH	WICHICH I	WIIIWA	1317

(2) INFORMATION FOR SEQ ID NO:73:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 648 base pairs
- 55 (B) TYPE: nucleic acid

480

540

600

```
(C) STRANDEDNESS: double
               (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
        (iii) HYPOTHETICAL: NO
         (iv) ANTI-SENSE: NO
10
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
               (A) NAME/KEY: misc_feature
15
               (B) LOCATION 1...648
        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:
     ATGCAAGCGT TAAAATCATT GCTTGAAGTG ATTACAAAAC TCCAGAATCT AGGCGGCTAT
     TTGATGCATA TAGCTATTTT CATCATTTTT ATTTGGATTG GAGGGCTTAA GTTTGTGCCT 120
20
     TACGAAGCTG AAGGGATCGC CCCTTTTGTG GCCAACTCCC CTTTCTTTTC TTTCATGTAT
     AAATTTGAAA AACCTGCATA CAAACAACAC AAAATGTCTG AATCCCAATC CATGCAAGAA
     GAAATGCAAG ATAACCCTAA AATCGTTGAA AACAAAGAAT GGCATAAAGA AAACCGCACT
     TATTTAGTGG CTGAAGGTTT AGGGATTACG ATCATGATCC TAGGCATTTT GGTGCTTTTG
     GGGCTTTGGA TGCCTTTAAT GGGCGTAGTT GGGGGCTTGC TTGTCGCTGG AATGACGATC
     ACCACCCTAT CTTTTTTATT CACAACGCCA GAAGTGTTTG TCAATCAGCA TTTCCCATGG
     CTTTCTGGGG CTGGAAGGCT AGTGGTTAAA GACTTGGCGT TATTTGCTGG AGGCTTGTTT
     GTGGCCGGAT TTGATGCGAA ACGCTATTTG GAGGGTAAAG GGTTTTGCTT GATGGACCGC
     TCATCGGTAG GGATTAAAAC TAAATGCTCT AGCGGGTGTT GCTCTTAA
30
     (2) INFORMATION FOR SEQ ID NO:74:
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 186 amino acids
35
               (B) TYPE: amino acid
               (D) TOPOLOGY: linear
         (ii) MOLECULE TYPE: protein
40
        (iii) HYPOTHETICAL: YES
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
45
         (ix) FEATURE:
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...186
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:
50
    Met Ile Lys Arg Ile Ala Cys Ile Leu Ser Leu Ser Ala Ser Leu Ala
                                        10
    Leu Ala Gly Glu Val Asn Gly Phe Phe Met Gly Ala Gly Tyr Gln Gln
                                    25
55 Gly Arg Tyr Gly Pro Tyr Asn Ser Asn Tyr Ser Asp Trp Arg His Gly
```

	•		35				F 3	40	•				45			
		50					55	Phe				60				
5	65					70		Val			75					80
	Thr	Ser	Gly	Thr	Glu 85	His	Thr	Lys	Thr	Asn 90	Leu	Leu	Thr	Tyr	Gly 95	Gl
	Gly	Gly	Asp	Leu 100	Ile	Val	Asn	Leu	Ile 105	Pro	Leu	Asp	Lys		Ala	Le
10	Gly	Leu	Ile 115	Gly		Val	Gln	Leu 120	Ala		Asn		Trp	Met	Phe	Pr
	Tyr	Asp 130			Gln	Thr	Arg	Phe		Phe	Leu			Leu	Gly	Gl
15	Arg		Arg	Val	Gly	Asp	135 Arg	Ser	Ala	Phe				Val	Lys	Phe
13		Met	Val	Asn	Gln	150 Gly	Ser	Lys	Asp			Leu	Ile	Arg	Tyr	160 Ty:
	Ser	Tro	Tvr	Val	165 Asp	የ ጉረጉ	Val	Phe	The	170					175	
20			,	180			vai	rne	185							
20	(2)	INFO	ORMA'	TION	FOR	SEQ	ID	NO : 7	5 :							
		(i)						ISTI				*				
25			. (2	A) LI	ENGT	1: 1:	16 a	mino	aci	ds						
23			- (1	D) T	YPE: OPOLO	amı DGY:	no a lin	cıd ear							•	
٠		(ii)	MO	LECUI	LE TY	PE:	pro	tein					•			
30		(iii)				•										
		•														
		(V1)			AL SO RGANI			icoba	acte	r pý	lori					
35		(ix)		TURI						•						
	•				AME/F CATI			c_fea 116	atur	e						
	•	(xi)	SEC	OUENC	E DE	SCRI	rp r t <i>(</i>	ON: S	SEO -	TT) NY	7.75			.*		
40																
	Τ.				5			Leu		10	*				15	
	Leu	Lys	Leu	Ala 20	Leu	Ala	Ser	Leu	Met 25	Gly	Gly	Leu	Trp	Tyr 30	Ala	Phe
1 5	Asn	Gly	Glu 35	Gly	Ser	Glu	Ile	Val		Ile	Gly	Ile	Phe 45	Val	Leu	Ile
	Leu	Phe 50		Phe	Phe	Ile	Arg 55	Pro	Val	Ser	Phe	Gln 60	Asp	Pro	Glu	Lys
50	Arg 65		Glu	Tyr	Ile	Glu 70		Leu	Lys	Lys		His	Glu	Arg	Lys.	
		Leu	Gln	Asp	Lys 85		Lys	Glu	Glu		75 Met	Arg	Leu	Tyr		80 Ala
	Lys	Lys	Glu	Arg 100		Ser	Arg	Gln		90 Gln	Asp	Leu	Lys		95 Gln	Met
55	Lys	Lys	Tyr						105					110		

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115

(2) INFORMATION FOR SEQ ID NO:76:

5 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 345 amino acids
(B) TYPE: amino acid

(D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

15 (A) ORGANISM: Helicobacter pylori

(ix) FEATURE:

(A) NAME/KEY: misc feature

(B) LOCATION 1...345

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

Met Val Lys His Tyr Leu Phe Met Ala Val Ser Gln Val Phe Phe Ser 25 Phe Phe Leu Val Leu Phe Phe Ile Ser Ser Ile Val Leu Leu Ile Ser Ile Ala Ser Val Thr Leu Val Ile Lys Val Ser Phe Leu Asp Leu Val 40 Gln Leu Phe Leu Tyr Ser Leu Pro Gly Thr Ile Phe Phe Ile Leu Pro 30 55 Ile Thr Phe Phe Ala Ala Cys Ala Leu Gly Leu Ser Arg Leu Ser Tyr 70 75 Asp His Glu Leu Leu Val Phe Phe Ser Leu Gly Val Ser Pro Lys Lys 85 90 35 Met Thr Lys Ala Phe Val Pro Leu Ser Leu Leu Val Ser Ala Ile Leu Leu Ala Phe Ser Leu Ile Leu Ile Pro Thr Ser Lys Ser Ala Tyr Tyr 120 Gly Phe Leu Arg Gln Lys Lys Asp Lys Ile Asp Ile Asn Ile Arg Ala 135 Gly Glu Phe Gly Gln Lys Leu Gly Asp Trp Leu Val Tyr Val Asp Lys 150 Thr Glu Asn Asn Ser Tyr Asp Asn Leu Val Leu Phe Ser Asn Lys Ser Leu Ser Gln Glu Ser Phe Ile Leu Ala Gln Lys Gly Asn Ile Asn Asn 185 Gln Asn Gly Val Phe Glu Leu Asn Leu Tyr Asn Gly His Ala Tyr Phe 200 205 Thr Gln Gly Asp Lys Met Arg Lys Val Asp Phe Glu Glu Leu His Leu 50 215 Arg Asn Lys Leu Lys Ser Phe Asn Ser Asn Asp Ala Ala Tyr Leu Gln 235 Gly Thr Asp Tyr Leu Gly Tyr Trp Lys Lys Ala Phe Gly Lys Asn Ala

250

Asn Lys Asn Gln Lys Arg Arg Phe Ser Gln Ala Ile Leu Val Ser Leu

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				0.50												
	Dhe	Pro	I.eu	260 Ala	Ser	Val	Dhe	T.e.11	265	Dro	T.a.ı	Dhe	Gly	270	λl-	λαν
			275					280					285			
5		Arg 290					295					300				
	Gly 305	Val	Tyr	Phe	Leu	Met 310	Val	His	Val	Ile	Ser 315	Thr	Asp	Leu	Phe	Leu 320
	Met	Thr	Phe	Phe	Phe 325	Pro	Phe	Ile	Trp	Ala 330	Phe	Ile	Ser	Tyr	Leu 335	Leu
0	Phe	Arg	Lys	Phe 340	Ile	Leu	Lys	Arg	Tyr 345							
	(2)	INF	ORMA!	TION	FOR	SEQ	ו מג	NO: 7	7:/							
[5	•	(i)	(1	QUENCA) LI B) T	ENGTI YPE :	H: 2° amin	76 at	mino cid		is						
20		(ii)	MO	LECU	LE T	YPE:	pro	tein			•					
		(iii;)	HY	POTH	ETIC	AL: Y	YES									
25		(vi)		IGINA A) OI				icoba	acte	r py:	lori					
		(ix)	()	ATURI A) NZ B) L	AME/I				ature	€ .						
30		(xi)	SE	QUEN	CE DI	ESCR.	IPTIC	ON: S	SEQ :	ID NO	D:77	:				
	Met 1	Lys	Lys	Lys	Ala 5	Lys	Val	Phe	Trp	Суs 10	Cys	Phe	Lys	Met	Ile 15	Arg
35	Trp	Leu	Tyr	Leu 20	Ala	Val	Phe	Phe	Leu 25	Leu	Ser	Val	Ser	Asp 30	Ala	Lys
	Glu	Ile	Ala 35	Met	Gln	Arg	Phe	Asp 40	Lys	Gln	Asn	His	Lys 45	Ile	Phe	Glu
10	Ile	Leu 50	Ala	Asp	Lys	Val	Ser 55	Ala	ГÀЗ	Asp	Asn	Val 60	Ile	Thr	Ala	Ser
	Gly 65	Asn	Ala	Ile	Leu	Leu 70	Asn	Tyr	qaA	Va1	Tyr 75	Ile	Leu	Ala	Asp	Lys 80
	Val	Arg	Tyr	Asp	Thr 85	Lys	Thr	Lys	Glu	Ala 90	Leu	Leu	Glu	Gly	Asn 95	
15	Lys	Val	Tyr	Arg 100		Glu	Gly	Leu	Leu 105		Lys	Thr	Asp	Tyr 110		Lys
	Leu	Ser	Leu 115	Asn	Glu	Lys	Tyr	Glu 120	Ile	Ile	Phe	Pro	Phe 125	Tyr	Val	Gln
50		Ser 130					135	•		,		140				
	Asp 145	Gln	Lys	Tyr	Lys	Ile 150	Lys	Asn	Met	Ser	Ala 155	Ser	Gly	Cys	Ser	Ile 160
	Asp	Asn	Pro	Ile	Trp 165	His	Val	Asn	Ala	Thr 170	Ser	Gly	Ser	Phe	Asn 175	Met
55	${\tt Gln}$	Lys	Ser	His	Leu	Ser	Met	Trp	Asn		Lys	Ile	Tyr	Val		Asp

	71 -	B	17-7	180	Ma	T 011	Dwo	TT2	185	Dha	Mot	C	Mb so	190	7	T
		•	195	Leu				200					205			
5	_	210		Gly			215				7	220				_
	225	•		Tyr		230	•		-		235	*				240
	-				245					250	_	_	_		255	
10				Ala 260	Arg	Tyr	Ile	Asn	Ser 265		Thr	Gln	Val	Phe 270	Ile	Gln
	Cys	Ala	Leu 275	Phe												
15	(2)	INF	ORMA'	TION	FOR	SEQ	ID 1	NO: 78	3:							
		(i)		QUEN						_						
				A) Li B) Ti					acio	is						
20				D) T												
		(ii)) MO	LECUI	LE T	YPE:	pro	tein								
25		(iii)	HY!	POTH	ETIC	AL: Y	YES									
		(vi)		IGINA A) OI				icoba	acte	r py:	lori	•				
30		(ix)	(2	ATURI A) Ni B) L	AME/I			_	ature	€		,				
		(xi)) SE	QUEN	CE DI	ESCR:	[PTI	ON: S	SEQ :	ID NO	0:78	•				
35	Met 1	Ile	Arg	Leu	Lys 5	Gly	Leu	Asn	Lys	Thr	Leu	Lys	Thr	Ser	Leu 15	Leu
	Ala	Gly	Val	Leu 20	Leu	Gly	Ala	Thr	Ala 25	Pro	Leu	Met	Ala	Lys 30	Pro	Leu
40	Leu	Ser	Asp 35	Glu	Asp	Leu	Leu	Lys 40	Arg	Val	Lys	Leu	His 45	Asn	Ile	Lys
	Glu	Asp 50	Thr	Leu	Thr	Ser	Cys 55	Asn	Ala	Lys	Val	Asp 60	Gly	Ser	Gln	Tyr
	Leu 65	Asn	Ser	Gly	Trp	Asn 70	Leu	Ser	Lys	Glu	Phe 75	Pro	Gln	Glu	Tyr	Arg 80
45	Glu	Lys	Ile	Phe	Glu 85	Cys	.Val	Glu	Glu	Glu 90	Lys	His	Lys	Gln	Ala 95	Leu
	Asn	Leu	Ile	Asn 100	Lys	Glu	Asp	Thr	Lys 105	Asp	Lys	Glu	Glu	Leu 110	Ala	Lys
50			115	Glu		-		120		_			125		-	
	Met	Ala 130	Phe	Glu	Met	Lys	Glu 135	His	Ser	Lys	Glu	Phe 140	Pro	Asn	Lys	Lys
	Gln 145	Leu	Gln	Thr	Met	Leu 150	Glu	Asn	Ala	Phe	Asp 155	Asn	Gly	Ala	Glu	Ser 160

Phe Ile Asp Asp Trp His Glu Arg Phe Gly Gly Ile Ser Arg Glu Asn

					165					170		•			175		
	Thr	Tyr	Lys	Ala 180	Leu	Gly	Ile	Lys	Glu 185	Tyr	Ser	Asp	Glu	Gly 190	Lys	Ile	
5	Leu	Pro	Leu 195	Ala	Lys.	Glu	Val	Ile 200	Leu	Asp	Asn	Ile	Lys 205	Lys	Ile	Leu	
	Lys	Lys 210	Ala	Leu	Met	Ile	Leu 215	Asp	Asn	Pro	Tyr	Leu 220	Leu	Trp	Leu	Val	
10	(2)	INF	ORMA'	rion	FOR	SEQ	ID 1	NO:7	9:								
		· (i)	(2	A) L	engti	HARA(H: 42	29 ar	mino		ds .							
15						amir OGY:											
15		(ii)) MOI	LECU	LE T	YPE:	prot	tein		•					•		
		(iii)	HY:	POTH	ETIC	AL: 3	/ES										
20		(vi)				OURCI		icoba	acte	г ру	lori						
. -		(ix)	(2		AME/1	KEY:			atur	e		•					
25						ION :								-		٠	
						ESCR:											
30	1				5	Arg				10					15	-	
				20		Met			25					30	•		
25			35			Ala		40					45				
35	Ser	50					55					60 -					
	65					Asp 70					75	٠.			*	80	
40					85	Leu				90					95		
				100					105					110			
	Leu	Leu	Pro 115	Lys	Lys	Val	Val	Gly 120	Arg	Tyr	Ala	Ile	Leu 125	Val	Met	Asn	
45	Thr	Leu 130	Leu	Ala	Tyr	Leu	Asn i35	Thr	Arg	Asn	Asn	Asp 140	Phe	Asn	Ile	Gln	
	Val 145	Phe	Asp	Ser		Glu 150	Glu	Ser	Pro	Glu	Lys 155		Glu	Glu	Thr	Tyr 160	
50	Lys	Glu	Ile	Glu	Lys 165	Glu	Lys	Phe	Pro	Phe 170	Ile	Ile	Ala	Leu	Leu 175		
	Lys	Glu	Gly	Val 180	Glu	Asn	Leu		Gln 185		Thr	Thr	Ile	Asn 190		Pro	
	Thr	Tyr	Val 195	Pro	Thr	Val	Asn			Gln	Leu	Glu	Asn 205	His	Thr	Glu	
55	Leu	Ser	Leu	Ser	Glu	Arg	Leu		Phe	Gly	Gly	Ile			Lys	Glu	

		210					215	٠				220				
	225		-	Met		230					235					240
5		-	_	Asp	245					250					255	
				Asn 260					265					270		
			275	Ser		,		280					285			
10 .	-	290		Thr			295					300				
		Leu	Ser	Gln	Ile		Leu	Leu	Glu	Tyr		Pro	Leu	Lys	Ile	
•	305	m\	01 -	7 3	3	310	7.00	Ď.mo	C.~~	T 033	315	T 011	T.033	Thr	Gln	320 Bro
15				Ile	325					330					335	
	Lys	Asp	Arg	Lys	Asn	Leu	Phe	IIe	Val 345	Asn	ALA	Leu	GIN	350	ser	Asp
	C1	Thr	T.eu	340 Ile	Gli	Type	Δla	Ser		T.e.u	Gli	Ser	Asp		Arσ	His
	GIU	TIII	355	116	GIU	TYL	ALG	360	DCG	Deu	GIU	501	365			
20	Asp	Trp 370		Asn	Tyr	Ser	Ser 375		Ile	Gly	Leu	Glu 380		Phe	Leu	Asn
	Thr		Asp	Pro	His	Phe		Lys	Ser	Phe	Gln	Glu	Ser	Leu	Glu	Asp
	385	,	•			390	-	-	*		395					400
25 .	Asn	Gln	Val	Arg	Tyr 405	His	Asn	Gln	Ile	Tyr 410		Ala	Leu	Gly	Tyr 415	Ser
	Phe	Glu	Pro	Ile 420	Lys	Asn	Glu	Ser	Glu 425	Thr	Lys	Lys	Glu			
	(2)	TNF	амяс	TION	FOR	SEO	ID I	NO : 8	0 :							
30	(2)		J				'									
		(i)) SE	QUEN	CE C	HARA	CTER	ISTI	CS:							
			•	A) L					aci	ds						
			-	B) T												
35	•		(D) T	OPOL	OGY:	lin	ear								
33		(ii) MO	LECU	LĘ T	YPE:	pro	tein								
,		(iii) HY	POTH	ETIC	AL:	YES									
40		(vi) OR	IGIN	AL S	OURC	E:								·	
		••-		A) O				icob	acte	r py	lori				-	
		(ix	•	ATUR				_			•	. *				
45			•	A) N B) L				_	acur	е						
•		(xi) SE	QUEN	CE D	ESCR	IPTI	ON:	SEQ	ID N	O:80	:				
	77 <u>~</u> 7	T	T ••-	Phe	(1=	Tara	T.e.	Dro	T.a.r	ī,e;	Dhe	υ=1	Ser	Tle	ررم [Tvr
50	Val	ьeu	ьys	rne	5 5	. "ys	ьeu	Fro	neu	10	. FIIG	val	PET	116	15	- y -
		Gln	Ser	Pro	Leu	Leu	Ala	Phe	Asp 25	Tyr	Lys	Phe	Ser	Gly 30	Val	Ala
	Glu	Ser	Val		ГÀа	Val	Gly	Phe 40	Asn	His	Ser	Lys	Leu 45	Asn	Ser	Lys
~ ~										1	en1		mL		T	Y

											•					
		50					55					60				
	Gln	Val	Asp	Ser	Asn	Leu	Leu	Pro	Lys	Asn	Ile	Glu	Lys	His	Ser	Leu
	65		-			70			•		75		•			80
	Lys	Ile	Gly	Val	Gly	Gly	Ile	Leu	Gly	Ala	Leu	Ala	Tyr	Asp	Ser	Thr
5	•		-		85				•	90				-	95	
	Lvs	Thr	Leu	Ile	qaA	Gln	Ala	Thr	His	Gln	Ile	Tyr	Gly	Ser	Glu	Leu
				100	•				105			•	•	110		
	Phe	Tvr	Leu	Ile	Gly	Arg	Trp	Trp	Gly	Phe	Leu	Glv	Asn	Ala	Pro	Trp
*		. •	115		-	•	-	120	. •			•	125			•
10	Lvs	Asp		Leu	Ile	Glu	Ser		Ala	His	Thr	Arg		Tvr	Val	Leu
	2-	130					135					140		- 2		
•	Tvr		Ser	Tyr	Leu	Phe	Tvr	Ser	Tvr	Glv	Asp			His	Leu	Lvs
•	145			-1-		150	-1-	-	-1-	_	155	-1-				160
		Glv	Ara	Tyr	Leu		Asn	Met	Asp			Ser	Ser	Tvr	Thr	
15		1		-1-	165					170				-1-	175	
	Glv	Phe	Glu	Leu		Tvr	Lvs	Ile	Asn		Lvs	Ile	Ala	Leu		Tro
	2			180	•	•	-4		185					190	-2 -	
	Phe	Ser	Ser	Phe	Glv	Arq	Ala	Leu		Phe	Glv	Gln	Tro		Ara	Asp
			195		2			200			1		205		3	
20	Trp	Tvr		Pro	Ile	Val	Thr		Asp	Glv	Arg	Lvs		Val	Tvr	Asp
		210					215				5	220			- 4 -	_
	Glv			Ala	Ala	Gln		Tvr	Phe	Ser	Ser		His	Val	Gln	Val
	225					230		-2			235	-1-				240
		Pro	Phe	Ala	Tvr		Ser	Pro	Lvs	Ile		Glv	Ala	Pro	Glv	
25					245				•	250	- 4 -				255	
	Lvs	Ile	His	Ile	Asp	Ser	Asn	Pro	Lvs		Lvs	Gly	Leu	Gly		Arq
	-			260	•				265	•	•	•		270		
	Ala	Gln	Thr	Thr	Ile	Asn	Val	Ile	Phe	Pro	Val	Tyr	Ala	Lys	Asp	Leu
			275					280				•	285	•	-	
30	Tyr	Asp	Val	Tyr	Trp	Arg	Asn	Ser	Lys	Ile	Gly	Glu	Trp	Gly	Ala	Ser
	-	290		-	-	_	295		-		-	300	_	_		
	Leu	Leu	Ile	His	Gln	Arg	Phe	Asp	Tyr	Asn	Glu	Phe	Asn	Phe	Gly	Phe
	305					310		_			315					320
	Gly	Tyr	Tyr	Gln	Asn	Phe	Gly	Asn	Ala	Asn	Ala	Arg	Ile	Gly	Trp	Tyr
35					325					330					335	
	Gly	Asn	Pro	Ile	Pro	Phe	Asn	Tyr	Arg	Asn	Asn	Ser	Val	Tyr	Gly	Gly
				340					345			*		350		
	Val	Phe	Ser	Asn	Ala	Ile	Thr	Ala	Asp	Ala	Val	Ser	Gly	Tyr	Val	Phe
			355					360					365			
40	Gly	Gly	Gly	Val	Tyr	Arg	Gly	Phe	Leu	Trp	Gly	Ile	Leu	Gly	Arg	Tyr
		370					375					380				
	Thr	Tyr	Ala	Thr	Arg	Ala	Ser	Glu	Arg	Ser	Ile	Asn	Leu	Asn	Leu	Gly
	385	•		•		390					395		**			400
	Tyr	Lys	Trp	Gly	Ser	Phe	Ala	Arg	Val	Asp	Val	Asn	Leu	Glu	Tyr	Tyr
45					405					410					415	
	Val	Val	Ser	Met	His	Asn	Gly	Tyr	Arg	Leu	Asp	Tyr	Leu	Thr	Gly	Pro
				420					425					430		
	Phe	Asn	Lys	Ala	Phe	Lys	Ala	Asp	Ala	Gln	Asp	Arg	Ser	Asn	Leu	Met
			435					440					445			•
50	Val	Ser	Met	Lys	Phe	Phe	Phe									
		450				•	455									
													•			

- (2) INFORMATION FOR SEQ ID NO:81:
- 55 (i) SEQUENCE CHARACTERISTICS:

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(A) LENGTH: 282 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: YES (vi) ORIGINAL SOURCE: 10 (A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc feature (B) LOCATION 1...282 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:81: Met Gly Cys Ser Phe Ile Phe Lys Lys Val Arg Val Tyr Ser Lys Met 20 Leu Val Ala Leu Gly Leu Ser Ser Val Leu Ile Gly Cys Ala Met Asn 25 Pro Ser Ala Glu Thr Lys Lys Pro Asn Asp Ala Lys Asn Gln Gln Pro Val Gln Thr His Glu Arg Met Thr Thr Ser Ser Glu His Val Thr Pro 25 55 60 Leu Asp Phe Asn Tyr Pro Val His Ile Val Gln Ala Pro Gln Asn His 70 His Val Val Gly Ile Leu Met Pro Arg Ile Gln Val Ser Asp Asn Leu 85 Lys Pro Tyr Ile Asp Lys Phe Gln Asp Ala Leu Ile Asn Gln Ile Gln 105 Thr Ile Phe Glu Lys Arg Gly Tyr Gln Val Leu Arg Phe Gln Asp Glu 120 Lys Ala Leu Asn Val Gln Asp Lys Lys Ile Phe Ser Val Leu Asp 35 135 Leu Lys Gly Trp Val Gly Ile Leu Glu Asp Leu Lys Met Asn Leu Lys 150 155 Asp Pro Asn Ser Pro Asn Leu Asp Thr Leu Val Asp Gln Ser Ser Gly 170 40 Ser Val Trp Phe Asn Phe Tyr Glu Pro Glu Ser Asn Arg Val Val His 185 Asp Phe Ala Val Glu Val Gly Thr Phe Gln Ala Ile Thr Tyr Thr Tyr 200 Thr Ser Thr Asn Asn Ala Ser Gly Gly Phe Asn Ser Ser Lys Ser Val 45 215 Ile His Glu Asn Leu Asp Lys Asn Arg Glu Asp Ala Ile His Lys Ile 230 235 Leu Asn Arg Met Tyr Ala Val Val Met Lys Lys Ala Val Thr Glu Leu 245 250 50 Thr Lys Glu Asn Ile Ala Lys Tyr Arg Asp Ala Ile Asp Arg Met Lys 265 Gly Phe Lys Ser Ser Met Pro Gln Lys Lys

55 (2) INFORMATION FOR SEQ ID NO:82:

		(1	.) SE													
								mino	aci	ds						
_						ami										
5			(D) T	OPOL	OGY:	lin	ear				•				
		122	١ ٧٠	T 17011							•					
		(11) MO	LECU	LE T	YPE:	pro	tein								
	٠	(111) HY	ם ייים	ייייייייייייייייייייייייייייייייייייי	7.1	VPC									
10		,	, 111	FOIR	Dir.C	ALI:	110		٠.							
		(vi) OR	IGIN	AL S	OTTRC	E.	•		•	٠.		•			
		•						icob	acte	r pv	lori				*	
				•						- 27						
		(ix) FE													
15								c_fe	atur	e						
			.(B) L	OCAT	ION	1	280								
		1		^	<u>~~ -</u>											
		(XI) SE	QUEN	CE D	ESCR	IPTI	ON:	SEQ	ID N	0:82	:				
20	Met.	Tvs	Leu	Ανα	Δla	Ser	17 - 1	1.011	T1.0	<i>~</i> 1	นาไ	77.	T 1.	7	G	.
_,	1	_,_		•	5	5 01	Val	neu	116	10	Val	ALA	TTE	Leu	Cys 15	те
	Ile	Leu	Ser	Ala	Cys	Ser	Asn	Tvr	Ala		Lvs	Val	Val	Lvs		Lar
				20	-				25	-1 -	-1-			30	0411	 ,
	Asn	His	Val	Tyr	Thr	Pro	Val	Tyr	Asn	Glu	Leu	Ile	Glu	Lys	Tyr	Se:
25			35					40					45		_	
	Glu	Ile	Pro	Leu	Asn	Asp		Leu	Lys	Asp	Thr	Pro	Phe	Met	Val	Glı
	17a l	50	T	D	•	****	55	_	_	_	_	60				
	65	Lys	Leu	Pro	Asn	79r	гÀг	Asp	Tyr	Leu		Asp	Asn	Lys	Gln	
30		Len	Thr	Dhe	Lve	. •	1721	Wi c	ui a	50.00	75	T	- 7-	m1		80
					85	Deu	val	птэ	urs	90	ьys	ьys	116	Inr	Leu 95	TIG
	Gly	Asp	Ala	Asn		Ile	Leu	Gln	Tvr		Asn	Tvr	Phe	Gln		Δαι
				100	_				105	2		-1-		110		
	Gly	Ala	Arg	Ser	Asp	Ile	Asp	Phe	Tyr	Leu	Gln	Pro	Thr		Asn	Glı
35			115					120					125			
	Lys	Gly	Val	Val	Met	Ile		Ser	Asn	Tyr	Asn	Asp	Asn	Pro	Asn	Ası
	T	130	*		~ 3	_,	135	_				140				
	Lys 145	GIU	Lys	Pro	Gin		Pne	Asp	Val	Leu		Gly	Ser	Gln	Pro	
40	_	Glv	Ala	Δgn	ጥh r	150	λen	Lou	uia	~1··	155	7		a	~ 1	160
		1		******	165	шys	ASII	Deu	ure	170	TYE	Asp	val	ser	175	Ala
	Asn	Asn	Lys	Gln		Ile	Asn	Glu	Val	Ala	Ara	Glu	Lvs	Δla	GJ n	T.A.
			_	180										190		
	Glu	Lys	Ile	Asn	${\tt Gln}$	Tyr	Tyr	Lys	Thr	Leu	Leu	Gln	Asp	Lys	Glu	Glr
45			195					200					205			
	Glu	Tyr	Thr	Thr	Arg	Lys		Asn	Gln	Arg	Glu	Ile	Leu	Glu	Thr	Let
٠.	0	210	.		~ 3.	_	215		_		•	220				
	225	ASII	Arg	ATA	GTA		GIn	Met	Arg	Gln		Val	Ile	Ser	Ser	
50		Dhe	Lve	Aen	Glv.	230	T 011	7	Mat	~ 1	235		~ 3	~ 3		240
	~~~		Lys		245	uoii	neu	usii	net	250	нтα	гуѕ	GIU	GIU		val
	Arg	Glu	Lys	Leu		Glu	Glu	Ara	Glu		Gl v	Tyr	Len	Ara	255 Asn	ري د اي
			-	260					265			-1-	u	270		UII.
	Ile	Arg	Ser	Leu	Leu	Ser	Gly	Lys								
55			275				_	280								

260

```
(2) INFORMATION FOR SEQ ID NO:83:
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 393 amino acids
               (B) TYPE: amino acid
               (D) TOPOLOGY: linear
        (ii) MOLECULE TYPE: protein
10
        (iii) HYPOTHETICAL: YES
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
15
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
               (B) LOCATION 1...393
20
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:
     Met Arg Lys Leu Phe Ile Pro Leu Leu Phe Ser Ala Leu Glu Ala
     Asn Glu Lys Asn Gly Phe Phe Ile Glu Ala Gly Phe Glu Thr Gly Leu
25
     Leu Glu Gly Thr Gln Thr Gln Glu Lys Arg His Thr Thr Thr Lys Asn
                                 40
     Thr Tyr Ala Thr Tyr Asn Tyr Leu Pro Thr Asp Thr Ile Leu Lys Arg
                             55
                                                 60
     Ala Ala Asn Leu Phe Thr Asn Ala Glu Ala Ile Ser Lys Leu Lys Phe
                         70
     Ser Ser Leu Ser Pro Val Arg Val Leu Tyr Met Tyr Asn Gly Gln Leu
                                         90
     Thr Ile Glu Asn Phe Leu Pro Tyr Asn Leu Asn Asn Val Lys Leu Ser
35
                                     105
     Phe Thr Asp Ala Gln Gly Asn Val Ile Asp Leu Gly Val Ile Glu Thr
                                 120
     Ile Pro Lys His Ser Lys Ile Val Leu Pro Gly Glu Ala Phe Asp Ser
                             135
    Leu Lys Ile Asp Pro Tyr Thr Leu Phe Leu Pro Lys Ile Glu Ala Thr
                         150
                                             155
     Ser Thr Ser Ile Ser Asp Ala Asn Thr Gln Arg Val Phe Glu Thr Leu
                                         170
     Asn Lys Ile Lys Thr Asn Leu Val Val Asn Tyr Arg Asn Glu Asn Lys
45
                                     185
     Phe Lys Asp His Glu Asn His Trp Glu Ala Phe Thr Pro Gln Thr Ala
                                 200
     Glu Glu Phe Thr Asn Leu Met Leu Asn Met Ile Ala Val Leu Asp Ser
                             215
50
     Gln Ser Trp Gly Asp Ala Ile Leu Asn Ala Pro Phe Glu Phe Thr Asn
                                             235
     Ser Pro Thr Asp Cys Asp Asn Asp Pro Ser Lys Cys Val Asn Pro Gly
                                        250
     Thr Asn Gly Leu Val Asn Ser Lys Val Asp Gln Lys Tyr Val Leu Asn
```

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Lys Gln Asp Ile Val Asn Lys Phe Lys Asn Lys Ala Asp Leu Asp Val
                                 280
     Ile Val Leu Lys Asp Ser Gly Val Val Gly Leu Gly Ser Asp Ile Thr
                             295
     Pro Ser Asn Asn Asp Gly Lys His Tyr Gly Gln Leu Gly Val Val
                        310
                                             315
     Ala Ser Ala Leu Asp Pro Lys Lys Leu Phe Gly Asp Asn Leu Lys Thr
                    . 325
                                         330
     Ile Asn Leu Glu Asp Leu Arg Thr Ile Leu His Glu Phe Ser His Thr
                                     345
     Lys Gly Tyr Gly His Asn Gly Asn Met Thr Tyr Gln Arg Val Pro Val
                                 360
     Thr Lys Asp Gly Gln Val Glu Lys Asp Ser Asn Gly Lys Pro Lys Asp
                             375
     Ser Asp Gly Leu Pro Tyr Asn Val Cys
15
     (2) INFORMATION FOR SEQ ID NO:84:
20
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 270 amino acids
               (B) TYPE: amino acid
               (D) TOPOLOGY: linear
25
         (ii) MOLECULE TYPE: protein
        (iii) HYPOTHETICAL: YES
         (vi) ORIGINAL SOURCE:
30
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...270
35
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:
    Met Lys Lys Phe Val Ala Leu Gly Leu Leu Ser Ala Val Leu Ser Ser
40
     Ser Leu Leu Ala Glu Gly Asp Gly Val Tyr Ile Gly Thr Asn Tyr Gln
     Leu Gly Gln Ala Arg Leu Asn Ser Asn Ile Tyr Asn Thr Gly Asp Cys
     Thr Gly Ser Val Val Gly Cys Pro Pro Gly Leu Thr Ala Asn Lys His
45
                             55
    Asn Pro Gly Gly Thr Asn Ile Asn Trp His Ser Lys Tyr Ala Asn Gly
    Ala Leu Asn Gly Phe Gly Leu Asn Val Gly Tyr Lys Lys Phe Phe Gln
50
    Phe Lys Ser Leu Asp Met Thr Ser Lys Trp Phe Gly Phe Arg Val Tyr
                                     105
    Gly Leu Phe Asp Tyr Gly His Ala Asp Leu Gly Lys Gln Val Tyr Ala
                                120
```

Pro Asn Lys Ile Gln Leu Asp Met Val Ser Trp Gly Val Gly Ser Asp

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	Leu 145		Ala	Asp	Ile	Ile 150	Asp	Lys	Asp	Asn	Ala 155	Ser	Phe	Gly	Ile	Phe
			Val	Ala	Ile 165	Gly	Gly	Asn	Thr	Trp 170		Ser	Ser	Ala	Ala 175	
5	Tyr	Trp		Glu 180		Ile	Ile	Glu	Ala 185		Gly	Pro	Asp	Val 190		Thr
	Pro	Thr	Tyr 195		Asn	Pro	Asn	Ala 200	Pro	Tyr	Ser	Thr	Asn 205	Thr	Ser	Thr
10		210				Trp	215					220				*
	225					Glu 230					235					240
					245	Gly				250					His 255	Leu
15	Lys	Arg	Asp	Tyr 260	Ser	Leu	Tyr	Leu	Gly 265	Tyr	Asn	Tyr	Thr	Phe 270		
	(2)	INF	ORMA!	rion	FOR	SEQ	ID 1	NO:8	5:							
20		·(i)	(1	A) LI B) T	ENGTI YPE :	HARA( H: 14 amir DGY:	40 ai	mino cid		ds						
25		(ii)	) MOI	ĻECUI	LE T	YPE:	pro	tein						•		
		(iii)	HYI	POTHI	ETIC	AL: Y	YES			•						
30		(vi)				OURCI ISM:		icoba	acte	r py:	lori					
35		(ix)		A) N	AME/I	KEY:			ature	9						
,,		(xi)	SEÇ	QUEN	CE DI	ESCRI	IPTIC	ON:	SEQ :	ID N	0:85	:				
	Met 1	His	Pro	Ile	Met 5	Phe	Ala	Tyr	Ile	Ala 10	Asn	Ala	Leu	Ala	Gln 15	Ala
10				20		Thr			25				_	30		
•		•	35			Ile		40					45			
15		50				Tyr	55					60				
	65			•		Ser 70					75					80
50			•		85	Gln				90					95	
,,,				100		Ile Met			105					110		
÷			115			Lys		120					125	MCL	116	men
55	-170	130	<b></b>	****	ny s	Lys	135	***	y	-uys	SGI	140				

# (2) INFORMATION FOR SEQ ID NO:86:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 256 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein

10

5

- (iii) HYPOTHETICAL: YES
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori

- (ix) FEATURE:
  - (A) NAME/KEY: misc_feature
  - (B) LOCATION 1...256
- 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:
  - Met Leu Gly Ser Val Lys Lys Ala Val Phe Arg Val Leu Cys Leu Gly

    1 5 10 15
- Ala Leu Cys Leu Cys Gly Gly Leu Met Ala Glu Gln Asp Pro Lys Glu
  25 25 25 30
- Leu Ile Phe Ser Gly Ile Thr Ile Tyr Thr Asp Lys Asn Phe Thr Arg
  - Ala Lys Lys Tyr Phe Glu Lys Ala Cys Lys Ser Asn Asp Ala Asp Gly
    50 55 60
- Cys Ala Ile Leu Arg Glu Val Tyr Ser Ser Gly Lys Ala Ile Ala Arg
  65 70 75 80
  - Glu Asn Ala Arg Glu Ser Ile Glu Lys Ala Leu Glu His Thr Ala Thr
    85
    90
- Ala Lys Val Cys Lys Leu Asn Asp Ala Glu Lys Cys Lys Asp Leu Ala

  100 105 110
  - Glu Phe Tyr Phe Asn Val Asn Asp Leu Lys Asn Ala Leu Glu Tyr Tyr
    115
    120
    125
  - Ser Lys Ser Cys Lys Leu Asn Asn Val Glu Gly Cys Met Leu Ser Ala
    130
    135
    140
- Thr Phe Tyr Asn Asp Met Ile Lys Gly Leu Lys Lys Asp Lys Lys Asp 145 150 155 160
  - Leu Glu Tyr Tyr Ser Lys Ala Cys Glu Leu Asn Asn Gly Gly Gly Cys
    165 170 175
- Ser Lys Leu Gly Gly Asp Tyr Phe Phe Gly Glu Gly Val Thr Lys Asp
  180 185 190
  - Phe Lys Lys Ala Phe Glu Tyr Ser Ala Lys Ala Cys Glu Leu Asn Asp
    195 200 205
  - Ala Lys Gly Cys Tyr Ala Leu Ala Ala Phe Tyr Asn Glu Gly Lys Gly
    210 215 220
- Val Ala Lys Asp Glu Lys Gln Thr Thr Glu Asn Leu Glu Lys Ser Cys
  225
  230
  235
  240
  - Lys Leu Gly Leu Lys Glu Ala Cys Asp Ile Leu Lys Glu Gln Lys Gln
    245 250 255
- 55 (2) INFORMATION FOR SEQ ID NO:87:

```
(i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 242 amino acids
               (B) TYPE: amino acid
 5
               (D) TOPOLOGY: linear
         (ii) MOLECULE TYPE: protein
        (iii) HYPOTHETICAL: YES
10
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
15
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...242
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:
20
     Met Lys Lys Phe Phe Ser Gln Ser Leu Leu Ala Leu Ile Ile Ser Met
                                         10
     Asn Ala Val Ser Gly Met Asp Gly Asn Gly Val Phe Leu Gly Ala Gly
                 20
                                     25
     Tyr Leu Gln Gly Gln Ala Gln Met His Ala Asp Ile Asn Ser Gln Lys
25
     Gln Ala Thr Asn Ala Thr Ile Lys Gly Phe Asp Ala Leu Leu Gly Tyr
     Gln Phe Phe Glu Lys His Phe Gly Leu Arg Leu Tyr Gly Phe Phe
                         70
30
     Asp Tyr Ala His Ala Asn Ser Ile Lys Leu Lys Asn Pro Asn Tyr Asn
                                         90
     Ser Glu Ala Ala Gln Val Ala Ser Gln Ile Leu Gly Lys Gln Glu Ile
                                     105
     Asn Arg Leu Thr Asn Ile Ala Asp Pro Arg Thr Phe Glu Pro Asn Met
35
                                 120
     Leu Thr Tyr Gly Gly Ala Met Asp Val Met Val Asn Val Ile Asn Asn
                            .135
                                                 140
     Gly Ile Met Ser Leu Gly Ala Phe Gly Gly Ile Gln Leu Ala Gly Asn
                         150
                                             155
40
     Ser Trp Leu Met Ala Thr Pro Ser Phe Glu Gly Ile Leu Val Glu Gln
                    165
                                        170
     Ala Leu Val Ser Lys Lys Ala Thr Ser Phe Gln Phe Leu Phe Asn Val
                                    185
     Gly Ala Arg Leu Arg Ile Leu Lys His Ser Ser Ile Glu Ala Gly Val
45
                                200
     Lys Phe Pro Met Leu Lys Lys Asn Pro Tyr Ile Thr Ala Lys Asn Leu
                            215
                                              220
     Asp Ile Gly Phe Arg Arg Val Tyr Ser Trp Tyr Val Asn Tyr Val Phe
```

(2) INFORMATION FOR SEQ ID NO:88:

230

55 (i) SEQUENCE CHARACTERISTICS:

50

Thr Phe

```
(A) LENGTH: 267 amino acids
```

(B) TYPE: amino acid

(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

10 (A) ORGANISM: Helicobacter pylori

(ix) FEATURE:

(A) NAME/KEY: misc_feature

(B) LOCATION 1...267

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

Met Asn Tyr Pro Asn Leu Pro Asn Ser Ala Leu Glu Ile Ser Glu Gln 10 Pro Glu Val Lys Glu Ile Thr Asn Glu Leu Leu Lys Gln Leu Gln Asn 20 25 Ala Leu Arg Ser Asn Ala His Phe Ser Glu Gln Val Glu Leu Ser Leu 40 Lys Cys Ile Val Arg Ile Leu Glu Val Leu Leu Ser Leu Asp Phe Phe 25 55 Lys Asn Ala Asn Glu Ile Asp Ser Ser Leu Arg Asn Ser Ile Glu Trp - 70 Leu Thr Asn Ala Gly Glu Ser Leu Lys Leu Lys Met Lys Glu Tyr Glu 85 90 Arg Phe Phe Ser Glu Phe Asn Thr Ser Met His Ala Asn Glu Gln Glu 30 100 105 Val Thr Asn Thr Leu Asn Ala Asn Ala Glu Asn Ile Lys Ser Glu Ile 120 Lys Lys Leu Glu Asn Gln Leu Ile Glu Thr Thr Thr Arg Leu Leu Thr 35 135 Ser Tyr Gln Ile Phe Leu Asn Gln Ala Arg Asp Asn Ala Asn Asn Gln 150 155 Ile Thr Lys Asn Lys Thr Gln Ser Leu Glu Ala Ile Thr Gln Ala Lys 165 170 40 Asn Asn Ala Asn Asn Glu Ile Ser Asn Asn Gln Thr Gln Ala Ile Thr 185 Asn Ile Thr Glu Ala Lys Thr Asn Ala Asn Asn Glu Ile Ser Asn Asn 200 205 Gln Thr Gln Ala Ile Thr Asn Ile Asn Glu Ala Lys Glu Ser Ala Thr 45 215 220 Thr Gln Ile Asn Ala Asn Lys Gln Glu Ala Ile Asn Asn Ile Thr Gln 230 235 Glu Lys Thr Gln Ala Thr Ser Glu Ile Thr Glu Ala Lys Lys Thr Asp 245 50 His Tyr Gln Asn Ile Asp Phe Phe Glu Phe Glu

- (2) INFORMATION FOR SEQ ID NO:89:
- 55 (i) SEQUENCE CHARACTERISTICS:

```
(A) LENGTH: 544 amino acids
               (B) TYPE: amino acid
               (D) TOPOLOGY: linear
         (ii) MOLECULE TYPE: protein
        (iii) HYPOTHETICAL: YES
         (vi) ORIGINAL SOURCE:
10
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
               (B) LOCATION 1...544
15
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:
     Val Ile Glu Thr Ile Pro Lys His Ser Lys Ile Val Leu Pro Gly Glu
20
    Ala Phe Asp Ser Leu Lys Glu Ala Phe Asp Lys Ile Asp Pro Tyr Thr
     Phe Phe Phe Pro Lys Phe Glu Ala Thr Ser Thr Ser Ile Ser Asp Thr
                                 40
     Asn Thr Gln Arg Val Phe Glu Thr Leu Asn Asn Ile Lys Thr Asn Leu
25
                             55
     Ile Met Lys Tyr Ser Asn Glu Asn Pro Asn Asn Phe Asn Thr Cys Pro
                         70
                                            75
     Tyr Asn Asn Asn Gly Asn Thr Lys Asn Asp Cys Trp Gln Asn Phe Thr
                  85
                                         90
30
    Pro Gln Thr Ala Glu Glu Phe Thr Asn Leu Met Leu Asn Met Ile Ala
                                     105
     Val Leu Asp Ser Gln Ser Trp Gly Asp Ala Ile Leu Asn Ala Pro Phe
                                 120
    Glu Phe Thr Asn Ser Ser Thr Asp Cys Asp Ser Asp Pro Ser Lys Cys
35
                             135
    Val Asn Pro Gly Val Asn Gly Arg Val Asp Thr Lys Val Asp Gln Gln
    Tyr Ile Leu Asn Lys Gln Gly Ile Ile Asn Asn Phe Arg Lys Lys Ile
                                        170
    Glu Ile Asp Ala Val Val Leu Lys Asn Ser Gly Val Val Gly Leu Ala
                                 185
    Asn Gly Tyr Gly Asn Asp Gly Glu Tyr Gly Thr Leu Gly Val Glu Ala
                                200
    Tyr Ala Leu Asp Pro Lys Lys Leu Phe Gly Asn Asp Leu Lys Thr Ile
45
                            215
    Asn Leu Glu Asp Leu Arg Thr Ile Leu His Glu Phe Ser His Thr Lys
                        230
                                            235
    Gly Tyr Gly His Asn Gly Asn Met Thr Tyr Gln Arg Val Pro Val Thr
                    245
                                        250
    Lys Asp Gly Gln Val Glu Lys Asp Ser Asn Gly Lys Pro Lys Asp Ser
                                    265
    Asp Gly Leu Pro Tyr Asn Val Cys Ser Leu Tyr Gly Gly Ser Asn Gln
                                280
    Pro Ala Phe Pro Ser Asn Tyr Pro Asn Ser Ile Tyr His Asn Cys Ala
```

	Asp 305	Val	Pro	Ala	Gly	Phe 310	Leu	Gly	Val	Thr		Ala	Val	Trp	Gln	Gln
			Asn	Gln	Asn		Leu	Pro	Ile	Asn	315 Tyr	Ala	Asn	Leu	Gly	320 Ser
5.	Gln	Thr	λen	Тъг	325	Len	λcm	7 J - 1		330	3	m\.	<b>~1</b>	•	335	
,				340				•	345					350		Ala
			355					360					365			Val
10	Thr	Asn	His	His	Phe	Ser		Ala	Ser	Gln	Ser			Ser	Pro	Ile
10	Leu	370 Glv	Val	Asn	Ala	ĭvs	375	Glv	Tarr	Gl n	7.00	380		2	3	Phe
	385	1				390	-16	GLY	ıyı	GIII	395	TAL	rne	ASII	Asp	400
	Ile	Gly	Leu	Ala	Tyr 405	Tyr.	Gly	Ile	Ile	Lys 410	Tyr	Asn	Tyr	Ala	Lys 415	Ala
15	Val	Asn	Gln	Lys 420	Val	Gln	Gln	Leu	Ser 425		Gly	Gly	Gly	Ile 430	Asp	Leu
-	Leu	Leu	Asp 435			Thr	Thr			Asn	Lys	Asn		Pro	Thr	Gly
20	Ile	Gln		Lys	Arg	Asn		440 Ser	Ser	Ser	Phe		445 Ile	Phe	Gly	Gly
20	Leu	450 Arq	Gly	Leu	Tvr	Asn	455 Ser	Tvr	ጥvጕ	Val	T.e.i	460	T.ve	Wal	Laro	C1
-	465					470					475					480
	Ser	Gly	Asn	Leu	Asp	Val	Ala	Thr	Gly		Asn	Tyr	Arg	Tyr	Lys	His
25	Ser	Lys	Tyr	Ser 500	485 Val	Gly	Ile	Ser		490 Pro	Leu	Ile	Gln		495 Lys	Ala
	Ser	Val	Val		Ser	Gly	Glv	Asp	505 Tvr	Thr	Agn	Ser	Dhe	510 Val	Dhe	λen
			<b>51</b> 5					520					525			
30	Glu	Gly 530	Ala	Ser	His	Phe	Lys 535	Val	Phe	Phe	Asn	Tyr 540	Gly	Gly	Cys	Phe
	(2)	INFO	RMAT	CION	FOR	SEQ	ID N	iO:90	):							
		(3)	e re	NT TENATO	ים כני	רא די	men e	ODT O								
35		(1)				IARAC I: 35				ls						
			(E	3) TY	PE:	amin	o ac	id								
			(E	)) TC	POLC	GY:	line	ar			٠					
40		(ii)	MOL	ECUL	E TY	PE:	prot	ein		٠		. ,				
·	(	iii)	HYP	OTHE	TICA	L: Y	ES									
		(vi)	ORT	CTNA	T. SO	URCE						٠				
_		( - /				SM:		coba	cter	pyl	ori	*				
45										• •						
		(IX)	FEA (A			EY:	misc	fea	turo			:				
						ON 1			cure						,	
50		(xi)	SEQ	UENC	E DE	SCRI	PTIO	N: S	EQ I	D NO	:90:					٠
	Leu	Met	Lys	Ser	Ile	Leu	Leu	Phe :	Met	Ile	Phe	Val	Val	Cys	Gln	Leu
	1				5					10					15	
55	Glu	ату	my ≈	ьуs 20	Lue	ser	ωin.		Asn 25	Phe	Lys	Val	Asp	Tyr 30	Asn	Tyr

•	Tyr	Leu	Arg 35	Lys	Gln	Asp	Leu	His 40	Ile	Ile	Lys	Thr	Gln 45	Asn	Asp	Leu
	Ser	Asn 50	Ala	Trp	Tyr	Leu	Pro 55	Pro	Gln	Lys	Ala	Pro 60	Lys	Glu	His	Ser
5	Trp 65	Val	Asp	Phe	Ala	Lys 70	Lys	Tyr	Leu	Asn	Met 75	Met	Asp	Tyr	Leu	Gly 80
	Thr	Tyr	Phe	Leu	Pro 85	Phe	Tyr	His	Ser	Phe 90	Thr	Pro	Ile	Phe	Gln 95	Trp
10				100					105					110		Gln
			115					120					125			Gly
		130					135				Trp	140	•		_	٠.
15		Pro	Gln	Ser	Ala				Met	Ile	Asn	Phe	Met	Pro	Glu	Leu
	145					150		• •	• * .		155					160
					165					170	Phe				175	
20				180					185		His			190		
			195					200			Lys		205			
		210					215				Lys	220				
25	225					230					Val 235					240
					245					250	Gly		_		255	
30				260					265		Ser			270		
			275					280			Asp		285			
		290			•		295				Phe	300				
35	305	•				310					Gly 315					320
					325					330	Phe				335	
40	Gly	Leu	Tyr	Glu 340	Tyr	Asp	Val	Phe	Ser 345	Asn	Arg	Ile	Gly	Val 350	Gly	Ile
	Arg	Leu	Asn 355	Pro			-									

(2) INFORMATION FOR SEQ ID NO:91:

45

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 675 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein
- (iii) HYPOTHETICAL: YES
- 55 (vi) ORIGINAL SOURCE:

# (A) ORGANISM: Helicobacter pylori

### (ix) FEATURE:

- (A) NAME/KEY: misc_feature
  (B) LOCATION 1...675

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

									-							
10	1				5					10					15	Ala
•				20					25					30		Ser
·			35	_		*		40					45			Asp
15	Ser	Leu 50	His	Phe	Lys	Val	Lys 55	Glu	Val	Gln	Ser	Val	Leu	Glu	Asn	Thr
•	Tyr 65	Thr	Ser	Met	Gly	Ile 70	Val	Lys	Glu	Met	Leu 75		Glu	Asp	Thr	Lys 80
20	Arg	Glu	Ile	Lys	Ile 85	Gln	Leu	Leu	Lys	Asn 90	Phe	Ile	Leu	Ala	Asn 95	Ser
-	His	Val	Ala	Gly 100	Val	Ser	Met	Phe	Phe 105	Lys	Asp	Arg	Glu	Asp	Leu	Arg
	Leu	Thr	Leu 115	Leu	Arg	Asp	Asn	Asp 120	Thr		Lys	Leu	Met 125	Glu	Asn	Pro
25	Ser	Leu 130	Gly	Ser	Asn	Pro	Leu 135	Ala		Lys	Ala	Met	Lys	Asn	Lys	Glu
	Ile 145	Ser	Lys	Ser	Leu	Pro 150		Tyr	Arg	Lys	Met 155		Asn	Gly	Ala	Glu 160
30	Val	Tyr	Gly	Val	Asp	Ile	Leu	Leu	Pro	Leu 170	Phe	Lys	Glu	Asn	Thr 175	Gln
	Glu	Val	Val	Gly 180	Val	Leu	Met		Phe		Ser	Ile	Asp	Ser	Phe	Ser
	Asn	Glu	Ile 195	Thr	Lys	Asn	Arg			Leu	Phe	Leu	Ile 205	Gly	Val	Lys
35	Gly	Lys 210	Val	Leu	Leu	Ser	Ala 215		Lys	Ser	Leu	Gln 220	Asp	Lys	Ser	Ile
	Thr 225	Glu	Ile	Tyr	Lys	Ser 230		Pro	Lys	Ala	Thr 235	Asn	Glu	Val	Met	
40	Ile	Leu	Glu	Asn			Lys	Ala	Thr	Leu 250	Glu	Tyr	Leu	Asp		240 Phe
	Ser	His	Lys	Glu 260		Phe	Leu	Ala	Val 265		Thr	Phe	Lys		255 Leu	Gly
	Lys	Thr	Glu 275		Lys	Asp	Asn	Leu 280		Trp	Met	Ile		270 Leu	Ile	Ile
45	Glu	Lys 290		Lys	Val	Tyr	Glu 295		Val	Gly	Ser		285 Arg	Phe	Val	Val
	Val 305		Ala	Ser	Ala	Ile 310		Val	Leu	Ala	Leu	300 Ile	Ile	Ala	Ile	
50		Leu	Met	Arg	Ala 325		Val	Ser	Asn		315 Leu	Glu	Val	Val		320 Ser
	Thr	Leu	Ser	His		Phe	Lys	Leu	Leu 345	330 Asn	Asn	Gln	Ala		335 Ser	Ser
	Asp	Ile	Lys 355		Val	Glu	Ala	Arg 360		Asn	Asp	Glu		350 Gly	Arg	Met
55	Gln	Thr		Ile	Asn	Lys	Asn		Leu	Gln	Thr	Gln	365 Lys	Thr	Met	Gln

(ix) FEATURE:

				•													
		370					375					380					
		Asp		Gln	Ala	Val		Asp	Thr	Ile	_		Val	Ser	Asp		
	385		<i>α</i> 1	7 cm	Dho	390		N	<b>T</b> 1.	Mlass	395	<b>a</b> 3	D		<b>a</b>	400	
5	цуз	ALA	GLY	Wan	405	Ala	vai	Arg	TTE	410	AIA	GIU	Pro	Ala	_	Pro	
	Asp	Leu	Lvs	Glu		Arg	Asp	Ala	Leu		Glv	Tle	Met	Δαη	415	T.eu	
			-1-	420		9		••••	425	1221	CLY	110	1100	430	- 7 -	Deu	
	Gln	Glu	Ser		Gly	Thr	His	Met	Pro	Ser	Ile	Phe	Lys		Phe	Glu	
			435		_			440					445				
10	Ser	Tyr 450	Ser	Gly	Leu	Asp	Phe 455	Arg	Gly	Arg	Ile	Gln 460	Asn	Ala	Ser	Gly	
	Arg	Val	Glu	Leu	Val	Thr	Asn	Ala	Leu	Gly	Gln		Ile	Gln	Lvs	Met	
	465					470					475					480	
15	Leu	Glu	Thr	Ser	Ser 485	Asn	Phe	Ala	Lys	Asp 490	Leu	Ala	Asn	Asp	Ser 495	Ala	
	Asn	Leu	Lys	Glu 500	Cys	Val	Gln	Asn	Leu 505	Glu	Lys	Ala	Ser	Asn 510	Ser	Gln	
	His	Lys	Ser	Leu	Met	Glu	Thr	Ser		Thr	Ile	Glu	Asn		Thr	Thr	
٠.		_	515					520		٠.			525			•	
20	Ser	Ile	Gln	Gly	Val	Ser	Ser	Gln	Ser	Glu	Ala	Met	Ile	Glu	Gln	Gly	
		530		_			535					540					
		Asp	Ile	Lys	Ser	Ile	Val	Glu	Ile	Ile		Asp	Ile	Ala	Asp		
	545	N cm	T on	T 011	77.	550	2	71-	7.1	<b>~</b> 7.	555			_		560	
25	1111	ASII	neu	пеп	565	Leu	ASII	Ara	Ala	570	GIU	Ата	Ala	Arg	575	GIĄ	
	Glu	His	Glv	Arg		Phe	Ala	Val	Val		Asn	Glu	Va1	Δτα		I.e.i	
				580					585		•			590			
	Ala	Glu	Arg 595	Thr	Gln	Lys	Ser	Leu 600	Ser	Glu	Ile	Glu	Ala 605	Asn	Ile	Asn	
30	Ile	Leu 610	Val	Gln	Ser	Ile	Ser 615	Asp	Thr	Ser	Glu	Ser 620	Ile	Lys	Asn	Gln	
	Val	Lys	Glu	Val	Glu	Glu		Asn	Ala	Ser	Ile		Ala	Leu	Arq	Ser	
	625					630					635				,	640	
	Val	Thr	Glu	Gly	Asn	Leu	Lys	Ile	Ala	Ser	Asp	Ser	Leu	Glu	Ile	Ser	
35	_	_			645					650			•		655		
	Gln	Glu	Ile		Lys	Val	Ser	Asn		Ile	Leu	Glu	Asp		Asn	Lys	
•	*	C1_	Dh -	660	•			•	665					670			
	гля	Gln	675														
40		-	0,5														
••	(2)	INFO	ORMA'	rion	FOR	SEQ	ID 1	NO: 92	2:								
		(i)	SEÇ	QUENC	E CI	IARAC	TER	STIC	2S :								
						I: 27			acid	ls							
45						amir											
,			(1	) TC	POLC	GY:	line	ear									
		(ii)	MOI	ECUI	E T	PE:	prot	ein			•						
50	. (	(iii)	нун	POTHE	TIC	AL: Y	ES.						•			٠	
		/ \	נמס	CTATE		VIII COP											
		(V1)				OURCE SM:		coba	cter	pyl	ori						

- (A) NAME/KEY: misc_feature
- (B) LOCATION 1...271

### (xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

Met Asn Ile Phe Lys Arg Ile Ile Cys Val Thr Ala Ile Val Leu Gly Phe Phe Asn Leu Leu Asp Ala Lys His His Lys Glu Lys Lys Glu Asp His Lys Ile Thr Arg Glu Leu Lys Val Gly Ala Asn Pro Val Pro His Ala Gln Ile Leu Gln Ser Val Val Asp Asp Leu Lys Glu Lys Gly Ile Lys Leu Val Ile Val Ser Phe Thr Asp Tyr Val Leu Pro Asn Leu Ala 15 75 Leu Asn Asp Gly Ser Leu Asp Ala Asn Tyr Phe Gln His Arg Pro Tyr 90 Leu Asp Arg Phe Asn Leu Asp Arg Lys Met His Leu Val Gly Leu Ala 100 105 20 Asn Ile His Val Glu Pro Leu Arg Phe Tyr Ser Gln Lys Ile Thr Asp 120 Ile Lys Asn Leu Lys Lys Gly Ser Val Ile Ala Val Pro Asn Asp Pro 135 Ala Asn Gln Gly Arg Ala Leu Ile Leu Leu His Lys Gln Gly Leu Ile 25 150 155 Ala Leu Lys Asp Pro Ser Asn Leu Tyr Ala Thr Glu Phe Asp Ile Val 170 Lys Asn Pro Tyr Asn Ile Lys Ile Lys Pro Leu Glu Ala Ala Leu Leu 185 30 Pro Lys Val Leu Gly Asp Val Asp Gly Ala Ile Ile Thr Gly Asn Tyr 200 Ala Leu Gln Ala Lys Leu Thr Gly Ala Leu Phe Ser Glu Asp Lys Asp 215 Ser Pro Tyr Ala Asn Leu Val Ala Ser Arg Glu Asp Asn Ala Gln Asp 230 235 Glu Ala Ile Lys Ala Leu Ile Glu Ala Leu Gln Ser Glu Lys Thr Arg 250 Lys Phe Ile Leu Asp Thr Tyr Lys Gly Ala Ile Ile Pro Ala Phe

(2) INFORMATION FOR SEQ ID NO:93:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 161 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- 50 (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Helicobacter pylori
- 55 (ix) FEATURE:

40

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(A) NAME/KEY: misc feature
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(B) LOCATION 1...161

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:

Met Phe Phe Lys Thr Tyr Gln Lys Leu Leu Gly Ala Ser Cys Leu Ala Leu Tyr Leu Val Gly Cys Gly Asn Gly Gly Gly Glu Ser Pro Val Glu Met Ile Ala Asn Ser Glu Gly Thr Phe Gln Ile Asp Ser Lys Ala 10 Asp Ser Ile Thr Ile Gln Gly Val Lys Leu Asn Arg Gly Asn Cys Ala Val Asn Phe Val Pro Val Ser Glu Thr Phe Gln Met Gly Val Leu Ser 15 Gln Val Thr Pro Ile Ser Ile Gln Asp Phe Lys Asp Met Ala Ser Thr 90 Tyr Lys Ile Phe Asp Gln Lys Lys Gly Leu Ala Asn Ile Ala Asn Lys 105 20 Ile Ser Gln Leu Glu Gln Lys Gly Val Met Met Glu Pro Gln Thr Leu 120 Asn Phe Gly Glu Ser Leu Lys Gly Ile Ser Gln Gly Cys Asn Ile Ile 135 140 Glu Ala Glu Ile Gln Thr Asp Lys Gly Ala Trp Thr Phe Asn Phe Asp 25 150

(2) INFORMATION FOR SEQ ID NO:94:

30

Lys

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 337 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein
- (iii) HYPOTHETICAL: YES
- 40
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
- (ix) FEATURE:
  - (A) NAME/KEY: misc_feature
- 45
- (B) LOCATION 1...337
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:
- Met Ile Arg Leu Lys Gly Leu Asn Lys Thr Leu Lys Thr Ser Leu Leu 50 10 Ala Gly Val Leu Leu Gly Ala Thr Ala Pro Leu Met Ala Lys Pro Leu 25 Leu Ser Asp Glu Asp Leu Leu Lys Arg Val Lys Leu His Asn Ile Lys 40 Glu Asp Thr Leu Thr Ser Cys Asn Ala Lys Val Asp Gly Ser Gln Tyr

	•	50					55					60	•				
	Leu	Asn	Ser	Gly	Trp	Asn	Leu	Ser	Lys	Glu	Phe	Pro	Gln	Glu	Tvr	Arg	
	65					70					75					80	
_	Glu	Lys	Ile	Phe	Glu	Cys	Val	Glu	Glu	Glu	Lys	His	Lys	Gln	Ala	Leu	
- 5					85					90					95		
	Asn	Leu	Ile	Asn	Lys	Glu	Asp	Thr	Glu	Asp	Lys	Glu	Glu	Leu	Ala	Lys	
				100	-				105					110			
	Lys	Ile	Lys	Glu	Ile	Lys	Glu	Lys	Ala	Lys	Val	Leu	Arg	Gln	Lys	Phe	
10			115			_		120					125				
10	Met	Ala	Phe	GIu	Met	Lys	Glu	His	Ser	Lys	Glu	Phe	Pro	Asn	Lys	Lys	
	<b>01</b> -	130		<b></b>		_	135		_			140					
	145	Leu	GIN	Thr	Met	Leu	GIu	Asn	Ala	Phe	Asp	Asn	Gly	Ala	Glu	Ser	
		T10	7 ~~	7		150	<b>~1</b>				155					160	
15	FIIC	116	ASP	wab	165	nis	GIU	Arg	Phe		Gly	Ile	Ser	Arg		Asn	
	Thr	Tvr	Targ	Δla		Glv	T10	T	<b>01</b>	170	_				175		
		- y -	Lly S	180	neu	GIY	116	Lys		Tyr	Ser	Asp	Glu		Lys	Ile	
	Leu	Ala	Phe		Glu	Δνα	Ser	Tyr	185	B	<b>71</b> -	m	•	190	_		
			195	1		,9	Jei	200	TIE	Arg	GII	Tyr		Lys	Asp	Phe	
20	Glu	Glu		Thr	Tvr	Asp	Thr	Arg	Gln	Thr	Lou	802	205	Mat	71-	<b>3</b>	
		210			•		215	• 9	0111	7 111	шец	220	Ald	met	ALA	ASN	
	Met.	Ser	Gly	Glu	Asn	Asp	Tyr	Lys	Ile	Thr	Tro	Len	Lve	Dro	Lare	т.	
	225					230	•	4			235	200	-75		цу	240	
	${\tt Gln}$	Leu	His	Ser	Ser	Asn	Asn	Ile	Lys	Pro	Leu	Met	Ser	Asn	Thr	Glu	
25					245					250					255		
	Leu	Leu	Asn	Met	Ile	Glu	Leu	Thr	Asn	Ile	Lys	Lys	Glu	Tyr	Val	Met	
				260					265					270			
	Gly	Cys	Asn	Met	Glu	Ile	Asp	Gly	Ser	Lys	Tyr	Pro	Ile	His	Lys	Asp	
30			275					280					285		•		
30	Trp	GIA	Phe	Phe	Gly	Lys	Ala	Lys	Val	Pro	Glu	Thr	Trp	Arg	Asn	Lys	
•	T10	290	<b>~1</b>	~	<b>-</b> 1 -		295	_				300					
	305	тър	GIU	Cys	iie	шуs 310	ASD	Lys	Val	Lys		Tyr	Asp	Asn	Thr	Thr	
		Glu	Tle	Glv	Tla		Tres	T	T		315	_	_			320	
35				<b>U</b>	325	Val	TLD	Lys	гуѕ		inr	lyr	Ser	IIe		His	
	His									330					335		
				•													
	(2)	INFO	RMAT	CION	FOR	SEQ	ID N	iO:95	:								
40																	
		(i)						STIC									
								ino	acid	s							
	*			) TY													
45			(I	) TO	POLO	GY:	line	ar									
43		,,,,				_	<i>:</i>										
		(11)	MOL	ECUL	E TY	PE:	prot	ein	·.								
	,		TTTO		m= a>	<u>.</u>											
		111)	nyP	OTHE	TTCA	ь: Y	ES										
50	·	(32i )	Орт	GINA	T CO	TÍD ČID											
J 0 .		· v ± /						k-		•							
			. (23	, Ore	GWIN T	SM:	uell	coba	cter	byr	ori						
		(ix)	FEA	TURE													
		/				EY:	misc	_fea	ture								
55			(B	) LO	CATI	ON 1	4	a 16									

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

5	Met 1	Lys	Lys	Leu	Val 5	Phe	Ser	Met	Leu	Leu 10	Cys	Cys	Lys	Ser	Val 15	Phe
	Ala	Glu	Gly	Glu 20	Thr	Pro	Leu	Ile	Val 25	Asn	Asp	Pro	Glu	Thr 30	His	Val
	Ser	Gln	Ala 35	Thr	Ile	Ile	Gly	Lys 40	Met	Val	Asp	Ser	Ile 45	Lys	Arg	Tyr
10	Glu	Glu 50	Ile	Ile	Ser	Lys	Ala 55	Gln	Ala	Gln	Val	Asn 60	Gln	Leu	Gln	Lys
	Val 65	Asn	Asn	Met	Ile	Asn 70	Thr	Thr	Asn	Ser	Leu 75	Ile	Ser	Ser	Ser	Ala 80
15					85	Pro				90					95	
••				100		Tyr			105					110		
20			115	•		Asn		120					125			
20	_	130				Val	135	•				140				
	145	-	_			Asn 150				-	155	-				160
25					165	Gln				170					175	
	_			180		Ser			185				_	190		_
30	_		195			Lys	,	200		_			205			
30		210				Thr	215					220		_		
•	225					Lys 230					235		-			240
35		-		_	245	Phe		_	_	250					255	
				260		Lys			265			_		270		
40			275			Arg	•	280					285			•
		290	_			Leu	295	-				300				
	305	200		204	1.00	310		275			315	2,5	an p		0111	320
	${\tt Gln}$	Ala	Tyr	Ala	Asn	Phe	Asn	Gln	Arg	Ile	Lys	Leu	Leu	Thr	Leu	Lys
45	_	_	_		325					330		_	_		335	
	_		•	340		Thr			345					350		
50			355			Ile		360			•		365			
30		370				Lys	375					380				
	385					Arg 390					395					400
55	АЗП	val	пÀя	FIIE	405	Gln	FIIC	GTÀ	FIIE	410	116	rne	ser	·TTG	415	чар

35

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(2) INFORMATION FOR SEQ ID NO:96:
          (i) SEQUENCE CHARACTERISTICS:
 5
               (A) LENGTH: 376 amino acids
               (B) TYPE: amino acid
               (D) TOPOLOGY: linear
         (ii) MOLECULE TYPE: protein
10
        (iii) HYPOTHETICAL: YES
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
15
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
               (B) LOCATION 1...376
20
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:
     Val Asn Lys Trp Ile Lys Gly Ala Val Val Phe Val Gly Gly Phe Ala
     Thr Ile Thr Thr Phe Ser Leu Ile Tyr His Gln Lys Pro Lys Ala Pro
25
     Leu Asn Asn Gln Pro Ser Leu Leu Asn Asp Asp Glu Val Lys Tyr Pro
                                 40
    Leu Gln Asp Tyr Thr Phe Thr Gln Asn Pro Gln Pro Thr Asn Thr Glu
```

55

135

215

70

150

230

85

165

245

100

Ser Ser Lys Asp Ala Thr Ile Lys Ala Leu Gln Glu Gln Leu Lys Ala

Ala Leu Lys Ala Leu Asn Ser Lys Glu Met Asn Tyr Ser Lys Glu Glu

Thr Phe Thr Ser Pro Pro Met Asp Pro Lys Thr Thr Pro Pro Lys Lys

Asp Asn Pro Asn Gly Ile Asp Ser Phe Thr Asn Leu Lys Glu Lys Asp

Ile Ala Thr Asn Glu Asn Lys Leu Leu Arg Thr Ile Thr Ala Asp Lys

Met Ile Pro Ala Phe Leu Ile Thr Pro Ile Ser Ser Gln Ile Ala Gly

Asn Asn Lys Met Gly Glu Tyr Arg Leu Asp Ile Val Trp Ser Arg Ile

Ile Thr Pro His Gly Ile Asn Ile Met Leu Thr Asn Ala Lys Gly Ala

Asp Ile Lys Gly Tyr Asn Gly Leu Val Gly Glu Leu Ile Glu Arg Asn

185 Lys Val Ile Ala Gln Val Glu Ser Asp Ile Phe Ala Ser Met Gly Lys 200 Ala Val Leu Ile Pro Lys Gly Ser Lys Val Ile Gly Tyr Tyr Ser Asn

105 Asp Phe Ser Pro Lys Gln Leu Asp Leu Leu Ala Ser Arg Ile Thr Pro 120 Phe Lys Gln Ser Pro Lys Asn Tyr Glu Glu Asn Leu Ile Phe Pro Val

90

170

250

Phe Gln Arg Tyr Gly Val Pro Leu Leu Ser Thr Leu Thr Asn Gly 280 Leu Leu Ile Gly Ile Thr Ser Ala Leu Asn Asn Arg Gly Asn Lys Glu 295 Glu Val Thr Asn Phe Phe Gly Asp Tyr Leu Leu Gln Leu Met Arg 310 315 Gln Ser Gly Met Gly Ile Asn Gln Val Val Asn Gln Ile Leu Arg Asp 330 Lys Ser Lys Ile Ala Pro Ile Val Val Ile Arg Glu Gly Ser Arg Val 10 345 Phe Ile Ser Pro Asn Thr Asp Ile Phe Phe Pro Ile Pro Arg Glu Asn 360 Glu Val Ile Ala Glu Phe Leu Lys 15 (2) INFORMATION FOR SEQ ID NO:97: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 916 amino acids 20 (B) TYPE: amino acid (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein 25 (iii) HYPOTHETICAL: YES (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori 30 (ix) FEATURE: (A) NAME/KEY: misc_feature · (B) LOCATION 1...916 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:97: 35 Val Asp Leu Arg Ile Gln Ser Lys Glu Val Ser His Asn Leu Lys Glu Leu Ser Lys Thr Leu Ile Ser Tyr Pro Phe Glu Lys His Val Glu Ala 40 Leu Gly Glu Gln Cys Ser Asn Phe Val Ser Ile Pro Ile Asn Asn Asp 40 Asp Tyr Ser Asn Ile Cys Thr Phe Val Ser Asp Phe Ile Asn Leu Ile Ala Ser Tyr Asn Leu Leu Glu Ser Phe Leu Asp Phe Tyr Lys Asp Lys 45 70 75 Leu Lys Leu Ser Glu Leu Val Thr Glu Tyr Ala Asn Val Thr Asn Asn 85 90 Leu Leu Phe Lys Lys Leu Ile Lys His Leu Ser Gly Asn Asn Gln Leu 105 Val Lys Asn Phe Tyr Gln Cys Ile Arg Glu Ile Ile Lys Tyr Asn Ala 120 Pro Asn Lys Glu Tyr Lys Pro Asn Gln Phe Phe Ile Ile Gly Lys Gly 135 140 Lys Gln Lys Gln Leu Ala Lys Ile Tyr Ser His Leu Lys Glu Leu Ser

٠.	Ala	Ser	Glu	Ile	Lys 165	Pro	Gln	Asp	Met	Glu 170	Asp	Ile	Leu	Lys	Lys 175	Leu
				180		Ile			185					190		
5	Pro	Lys	Thr 195	Glu	Ile	Lys	Asp	Ile 200		Lys	Glu	Ile	Asp 205	Glu	Lys	Tyr
		210				Phe	215					220				
10	225					Glu 230					235					240
* .					245	Ile			•	250					255	•
1.5				260		Tyr			265					270		
15			275					280					285			Ser.
		290				Met	295					300				
20	305					Glu 310					315					320
					325	Ser				330					335	
25				340		Leu			345					350	_	_
25			355			Lys		360					365			
		370				Cys	375					380				
30	385	urs	neu	ASII	TTG	Asn 390	ASI	GIŸ	Leu	ser	H15	Gin	Pne	GIu		Phe 400
					405	Glu				410					Asn 415	Asp
				420		Thr			425					430	Leu	
35			435			Gln		440					445			
		450				Ile	455					460				
40	465					Leu 470					475					480
	:				485	Tyr				490					495	
45				500					505					510		Ser
43			515			Asp		520					525			_
		530				Ala	535					540				
50	545					Ile 550					555					560
					565	Gln				570					575	
-55				580		Asn			585					590		
	****	JIU	-1E	ny s	neu	Glu	val	TÀL	ASP	cys	Arg	ьys	ser	HlS	ASP	HIS

			595					600					605			
	Asn	Glu	Pro	Ile	Ile	Leu	Ser	Gln	Gln	Ser	Thr	Gly	Phe	Gln	Trp	Ala
		610					615					620				
_	Phe	Asn	Phe	Met	Phe	Gly	Phe	Leu	Tyr	Asn	Val	Gly	Ser	His	Phe	Ser
5 -	625					630					635					640
	Phe	Asn	His	Asn	Ile	Ile	Tyr	Val	Met	_	Glu	Pro	Ala	Thr	His	Leu
					645					650					655	
	Ser	Val	Pro		Arg	Lys	Glu	Phe	-	Lys	Phe	Leu	Lys		Tyr	Ala
10	•••	•	<b>3</b>	660	17-7	m\	<b>5</b> 1-	1	665		<b></b> 1	••! -		670	_,	_
10	HIS	гÀа	675	HIS	Val	Thr	Pne	680	гел	Ala	Thr	HIS	_	Pro	Pne	Leu
	Val	) en	-	Δen	His	T.em	λen		Tla	7. ~~	Tla	1707	685	Tva	G1.,	Thr
	var	690	1111	Map	mis	пец	695	GIU	TTE	Arg	116	700	GLU	гуз	Gru	THE
	Glu		Ser	Val	Ile	Lvs		His	Phe	Asn	Tvr		Len	Asn	Asn	Δla
15	705	4				710					715					720
	Ser	Lys	Asp	Ser	Asp	Ala	Leu	Asp	Lys	Ile	Lys	Arg	Ser	Leu	Gly	Val
					725			_	-	730	-	•			735	
-	Gly	Gln	His	Val	Phe	His	Asn	Pro	Gln	Lys	His	Arg	Ile	Ile	Phe	Val
••				740					745					750		
20	Glu	Gly		Thr	Asp	Tyr	Cys		Leu	Ser	Ala	Phe		Leu	Tyr	Leu
	_	_	755			_	_	760	_				765		_	_
	Arg		ьуs	GIU	Tyr	Lys		Asn	Pro	He	Pro		Thr	Phe	Leu	Pro
	T10	770	Gl v	Lau	Lys	V C Z	775	602	7 ~~	7	Mat	780	C1	Mile se	T1.	<b>~</b> 3
25	785	Ser	GIY	Deu	цуз	790	дан	261	MSII	Asp	795	ьуѕ	GIU	1111	TTE	800
		Leu	Cvs	Glu	Leu		Asn	His	Pro	Tle		Lėn	Thr	Asp	Asn	
•	-4-		-1-		805					810					815	
	Arg	Lys	Cys	Val	Phe	Asn	Gln	Gln	Ala	Thr	Ser	Glu	Arg	Phe	Lys	Arg
				820					825					830		_
30	Ala	Asn	Glu	Glu	Met	His	Asp	Pro	Ile	Thr	Ile	Leu	Gln	Leu	Ser	Asp
			835		_			840					845			
	Cys		Arg	His	Phe	Lys		Ile	Glu	Asp	Cys		Ser	Ala	Asn	Asp
	3	850	, T	m	n 1	T	855	•	<b>~1</b>		~3	860	_			<b>5</b> 1
35	865	ASII	ьуs	Tyr	Ala	LуS 870	ASI	гÀг	GIN	Met		Leu	ser	Met	АТА	
33		Thr	Δτα	T.em	Leu		Glv	Glv	Glu	Acn	875	Tla	Glu	Laze	Gln	880 Thr
	275		9	DCu	885	+1-	OL y	·GIY	GIU	890	AIG	116	GIU	цуз	895	1111
	Lvs	Arq	Asn	Phe	Leu	Lvs	Leu	Phe	Lvs		Ile	Ala	Trp	Ala	-	Asn
	-4 .	3		900		-3 -			905					910		
40	Leu	Ile	Lys	Asn										-		
•			915													

### (2) INFORMATION FOR SEQ ID NO:98:

- 45 (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 176 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- 50 (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
- 55 (A) ORGANISM: Helicobacter pylori

```
(ix) FEATURE:
                (A) NAME/KEY: misc_feature
                (B) LOCATION 1...176
  5
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:
     Met Thr Ala Met Met Arg Tyr Phe His Ile Tyr Ala Thr Thr Phe Phe
                                          10
 10
     Phe Pro Leu Ala Leu Leu Phe Ala Val Ser Gly Leu Ser Leu Leu Phe
     Lys Ala Arg Gln Asp Thr Gly Ala Lys Ile Lys Glu Trp Val Leu Glu
     Lys Ser Leu Lys Lys Glu Glu Arg Leu Asp Phe Leu Lys Gly Phe Ile
15
     Lys Glu Asn His Ile Ala Met Pro Lys Lys Ile Glu Pro Arg Glu Tyr
     Arg Gly Ala Leu Val Ile Gly Thr Pro Leu Tyr Glu Ile Asn Leu Glu
     Thr Lys Gly Thr Gln Thr Lys Ile Lys Thr Ile Glu Arg Gly Phe Leu
20
     Gly Ala Leu Ile Met Leu His Lys Ala Lys Val Gly Ile Val Phe Gln
                                 120
     Ala Leu Leu Gly Ile Phe Cys Val Phe Leu Leu Phe Tyr Leu Ser
                           135
     Ala Phe Leu Met Val Ala Phe Lys Asp Thr Lys Arg Met Phe Ile Ser
                         150
                                             155
     Val Leu Ile Gly Ser Val Val Phe Phe Gly Ala Ile Tyr Trp Ser Leu
                                         170
30
     (2) INFORMATION FOR SEQ ID NO:99:
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 222 amino acids
35
               (B) TYPE: amino acid
               (D) TOPOLOGY: linear
         (ii) MOLECULE TYPE: protein
40
        (iii) HYPOTHETICAL: YES
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...222
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:
50
    Met Phe Lys Asn Ala Leu Asn Ile Gln Asp Phe Ser Phe Lys Asn His
    Thr Ser Thr Ala Ile Ile Gly Thr Asn Gly Ala Gly Lys Ser Thr Leu
55
     Ile Asn Thr Ile Leu Gly Ile Arg Ser Asp Tyr Asn Phe Lys Ala Gln
```

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			35					40					45			
	Asn	Asn	Asn	Ile	Pro	Tyr		Asp	Asn	Val	Ile	Pro	Gln	Arg	Lys	Gln
		50			_		55					60		_		
5		Gly	Val	Val	Ser		Leu	Phe	Asn	Tyr		Pro	GIA	Leu	Asn	
5	65	3	7 011	Dho	T 240	70 Dho	Пч гээ	<b>~1</b> ~	Dho	Dha	75 #40	T	7.55	C++C	Th~	80
	ASII	Asp	neu	Pile	ьув 85	FIIG	ıyı	GIII	PHE	90	птэ	пåэ	ASII	Cys	95	Ten
	Asn	Leu	Phe	Glu		Asn	Leu	Leu	Asn		Thr	Tvr	Glu	His		Šer
	rup	200		100	7				105	_		-1-		110		502
10	Asp	Gly	Gln		Gln	Arg	Leu	Lys				Ala	Leu	Ser	His	His
				. <del>-</del>				120		-			125			
								Glu	Pro	Glu	Thr	Ser	Leu	Glu	Gln	Asn
. •		130					135					140			•	
		Leu	Ile	Arg	Leu		Asn	Leu-	Ile	Ser		Arg	Asn	Thr	Gln	
15	145		_			150		1	<u>.</u>	_	155	<b>_</b>	_			160
	Leu	Thr	Ser	Ile		Ala	Thr	His	Asp		Ile	Val	Leu	Asp		
	<b>~1</b>	m	17-1	T 011	165	T 011	T	3 ~~	<i>α</i> 1	170	T1_	7.3.0		Tyr	175	
	GIU	ILD	vaı	180	Leu	reu	гуя	ASII	185		11e	ALA	GIII	190	гуя	Pro
20	Len	Asn	Ser	-	Leu	Lvs	Ser	Val		Lvs	Thr	Phe	Asn		Lvs	Glu
			195			-1-		200		-12			205	,	-,-	
	Lys	Pro	Thr	Thr	Lys	Asp	Leu	Leu	Ala	Leu	Leu	Lys	Asp	Ile		
	-	210			_	_	215					220	-			
25	(2)	INFO	ORMA'	LION	FOR	SEQ	ID 1	10:10	00:							
		(i)		OUEN												
				A) LI					acı	ıs						
30			•	3) TY O) T(												
30			,,	<i>)</i>	) F Q L	<b>J</b> G1 .	T T110	saı								
		(ii)	MOI	LECUI	LE T	YPE:	prot	ein								
		,					•								•	
		(iii)	HYI	POTH	ETIC	AL: 3	YES									
35																
		(vi)		IGIN							•					
			(2	7) ÓI	RGAN	ISM:	Hel:	Lcoba	acte	r py.	lori	•				•
					_											
40		(ix)		ATURI		rmar.				_						
40				A) NZ B) L(						3						
			1,	אני נכ	JUAI.	LON .	L <del>.</del>	100								
		(ri)	SEC	QUENC	ום אי	RSCR	דייים	)N - 9	SEO '	או כד	2-10	3 -				
:		(322)	,	202					Jug .			•				
45	Met	Tyr	Ala	Ala	His	Pro	Ile	Lys	Pro	·Ile	Lys	Ala	Pro	Lys	Leu	Lys
	1	•			5		•	•		10	•			•	15	•
	Ser	Gln	Phe	Leu	Arg	Arg	Val	Phe	Val	Gly	Ala	Ser	Ile	Arg	Arg	Trp
				20		_			25	=				30	-	_
	Asn	Asp	${\tt Gln}$	Ala	Cys	Pro	Leu	Glu	Phe	Val	Glu	Leu	Asp	Lys	Gln	Ala
50			35					40					45			
	His	-	Ala	Met	Ile	Ala	_	Leu	Leu	Ala	Lys	_	Leu	Lys	Asp	Arg
		50			_	_	55	_	_		_	60	_,	_		
		rys	Asp	ьеп	Asp		Asp	Leu	Leu	TTe		Tyr	Phe	Cys	Phe	
55	65 Dhe	Lev	<b>@1.</b> ,	A~~	Lev	70 Val	Len	Th~	y c.~	T1^	75	Dro	Dwa	Ile	Dha	80 Tur-
55	FIIC	neu	GIU	n.y	nen	var	⊥-cu	****	vah	T16	nys	LIO	PIO	TTG	LIIG	TAT

					85		•			90					95	
	Ala	Leu	Gln	Gln	Thr	His	Ser	Lys	Glu	Leu	Ala	Ser	Tyr	Val	Ala	Gln
				100					105					110		
_	Ser	Leu	Gln	Asp	Glu	Ile	Ser	Ala	Tyr	Phe	Ser	Leu	Glu	Glu	Leu	Lys
5			115					120					125			
	Glu	Tyr	Leu	Ser	His	Arg	Pro	Gln	Ile	Leu	Glu	Thr	Gln	Ile	Leu	Glu
		130					135					140				
	Ser	Ala	His	Phe	Tyr	Ala	Ser	Lys	Trp	Glu	Phe	Asp	Ile	Ile	Tvr	His
	145					150					155					160
10	Phe	Asn	Pro	Asn	Met	Tyr	Gly	Val	Lys	Glu	Ile	Lys	asp	Lvs	Ile	Asp
					165					170					175	
*	Lys	Gln	Leu	His	Asn	Asn	Asp	His	Leu	Phe	Glu	Gly	Leu	Phe	Glv	Glu
				180					185				-	190		
	Lys	Glu	Asp	Leu	Lys	Lys	Leu	Val	Ser	Met	Phe	Gly	Gln	Leu	Ara	Phe
15			195					200					205			
	Gln	Lys	Arg	Trp	Ser	Gln	Thr	Pro	Arg	Val	Pro	Gln	Thr	Ser	Val	Leu
	•	210					215					220				
	Gly	His	Thr	Leu	Cys	Val	Ala	Ile	Met	Gly	Tyr	Leu	Leu	Ser	Phe	Asp
•	225					230					235					240
20	Leu	Lys	Ala	Cys	Lys	Ser	Met	Arg	Ile	Asn	His	Phe	Leu	Gly	Gly	Leu
					245					250					255	
	Phe	His	Asp	Leu	Pro	Glu	Ile	Leu	Thr	Arg	Asp	Ile	Ile	Thr	Pro	Ile
	<b>-</b>	~-	_	260				•	265					270		
25	Lys	GIN	ser	val	Ala	GLY	Leu	Asp			Ile	Lys	Glu	Ile	Glu	Lys
23	T		275	<b>01</b> -	•	•		280					285			
	pas	290	Mec	GIR	Asn	гÀЗ		Tyr	Ser	Phe	Val		Leu	Gly	Val	Gln
	<i>c</i> 1		Ton	T	m	nL -	295	~~	_			300				
	305	veħ	Deu	гуу	TAT	310	Inr	Glu	Asn	GIU		Lys	Asn	Arg	Tyr	_
<b>30</b> .		Tare	Ser	Wic	Gln.		17-1	Db -	m1	<b>.</b>	315					320
-	p	_,5		****	325	116	val	Phe	III		Asp	Ата	GIu	GIu		Phe
	Thr	Len	Tvr	Asn		Aen	Gl 11	Tyr	T 011	330	17 1	<b>~</b>		<b>-1</b>	335	_
			-1-	340	501	r.sp	GIU	TYL.	345	GIY	vai	Cys	GIY		ьеи	Leu
	Lvs	Val	Cvs		His	Len	Ser	Ala		Low	C1	21-	a1-	350	0	<b>.</b>
35	-		355	<i>E</i>				360	1116	Deu	GIU	MIA	365	TTE	ser	Leu
	Ser	His	Gly	Ile	Ser	Ser	Tvr.	Asp	T.eu	Tle	Gln.	Gly		T 1/6	N 000	T 011
		370	•	_			375			-16	3111	380	Ta	nys	Well	neu
	Leu			Arg	Ser	Gln		Glu	Lev	Len	Agn	Len	Dan.	T.01	G1 1-	Tare
	385					390					395	u	· Here	-eu	GT Å	цуs 400
40	Leu	Phe	Arg	Asp	Phe							•				-200
•				_	405	•										
												•				:
	(2)	TNFC	רבאקו	MOT	FOP	SEO.	TD N	TO - 10					1			

### (2) INFORMATION FOR SEQ ID NO:101:

45 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 335 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

55 (A) ORGANISM: Helicobacter pylori

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### (ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION 1...335

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### (xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

		(11)	324	SORM	ים נו	JOCK.	LFIIC	JN	, <u>Q</u>	LD IN	J. 10.	• •				
	Va1	Leu	Tro	Val	Leu	Tvr	Phe	Leu	Thr	Ser	Leu	Phe	Ile	Cys	Ser	Leu
	1				5	-1-				10				-,-	15	
10	Ile	Val	Leu	_	Ser	Lys	Lys	Ser		Leu	Phe	Val	Asp	Asn	Ala	Asn
	•	<b>-</b> 1.	<b>71</b>	20	Db.	774 -	77.5		25	m\	D	3	<b>3</b> 1.	30	<b>a</b> 3	· • • • • •
•	•		35					40	•	-		•	45	•	-	Leu
15	Gly	Ile 50	Phe	Leu	Ser	Phe	Ala 55	Leu	Ala	Cys	Tyr	Leu 60	Glu	Pro	Phe	Glu
	Met 65	Pro	Phe	Lys	Gly	Pro 70	Phe	Val	Phe	Leu	Gly 75	Leu	Ser	Leu	Val	Phe 80
		Ser	Gly	Phe	Leu 85		Asp	Ile	Asn	Leu 90		Leu	Ser	Pro	Lys 95	
20	λνα	T.AII	т1ь	T.011		בומ	V=1	ėl v	Va I		Cve	Tla	Tla	Ser		Thr
20		٠.		100					105					110		
•	Pro	Leu	Val 115	Val	Sér	Asp	Phe	Ser 120	Pro	Leu	Phe	Ser	Leu 125	Pro	Tyr	Phe
-	Ile	Ala	Phe	Leu	Phe	Ala	Ile	Phe	Met	Leu	Val	Gly	Ile	Ser	Asn	Ala
25		130					135					140				
	Ile	Asn	Ile	Ile	Asp		Phe	Asn	Gly	Leu	Ala	Ser	Gly	Ile	Cys	
	145					150					155.		•			160
	Ile	Ala	Leu	Leu		Ile	His	Tyr	Ile	_	Pro	Ser	Ser	Leu		Cys
20	•	•	23-		165	37-3	7	<b>~</b> 3	Db	170	**- 3	•	<b>3</b>	Db	175	Ø
30	Leu	Leu	AIA	180	Mec	val.	Leu	GLY	185	Met	vaı	ьeu	Asn	190	Pro	ser
	Glv	Lare	Tla		T.em	Glv	Aen	G) v		λla	Тъг	Dho	Leu	Gly	T.au	1721
	,	_	195				_	200			_		205			
25	Cys		Ile	Ser	Leu	Leu		Leu	Ser	Leu	Glu		Lys	Ile	Ser	Val
35	_1	210	<b>~</b> 1			<b>.</b>	215		_	_		220	~ 1			<b>5</b> 1-
		Pne	GIY	Leu	ASI	230	met	Leu	Tyr	Pro		тте	GIU	Val	Leu	
	225	TIO	Lon	7 ~~	7~~		T1.	T ***	7~~	C1 n	235	77-	mp ~	Met	Dwo	240
40					245	٠.				250			٠		255	
40	Asn	Leu		Leu 260	His	Thr	Leu	Leu	Phe 265	Lys	Phe	Leu	Gln	Gln 270	Arg	Ser
	Phe	Asn	Tyr 275	Pro	Asn	Pro	Leu	Cys 280	Ala	Phe	Ile	Leu	Ile 285	Leu	Cys	Asn
	Leu	Pro		Ile	Leu	Ile	Ser		Leu	Phe	Arq	Leu		Ala	Tyr.	Ala
45		290					295					300	-		•	
	Leu	Ile	Val	Ile	Ser	Leu	Val	Phe	Ile	Ala	Cys	Tyr	Leu	Ile	Gly	Tyr
	305					310		•			315					320
	Ala	Tyr	Leu	Asn		Gln	Val	Cys	Ala		Glu	Lys	Arg	Ala		
50					325					330					335	
50																

(2) INFORMATION FOR SEQ ID NO:102:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 96 amino acids
- 55 (B) TYPE: amino acid

(D) TOPOLOGY	:/linear
--------------	----------

- (ii) MOLECULE TYPE: protein
- (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

- 10 (ix) FEATURE:
  - (A) NAME/KEY: misc_feature
  - (B) LOCATION 1...96
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

15 Met Lys Lys Val Ile Val Ala Leu Gly Val Leu Ala Phe Ala Asn Val

Leu Met Ala Thr Asp Val Lys Ala Leu Val Lys Gly Cys Ala Ala Cys

20 His Gly Val Lys Phe Glu Lys Lys Ala Leu Gly Lys Ser Lys Ile Val

Asn Met Met Ser Glu Lys Glu Ile Glu Glu Asp Leu Met Ala Phe Lys

- Ser Gly Ala Asn Lys Asn Pro Val Met Thr Ala Gln Ala Lys Lys Leu 25 75 Ser Asp Glu Asp Ile Lys Ala Leu Ala Lys Tyr Ile Pro Thr Leu Lys
- (2) INFORMATION FOR SEQ ID NO:103:

30

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 156 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear

35

- (ii) MOLECULE TYPE: protein
- (iii) HYPOTHETICAL: YES
- 40 (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:
    - (A) NAME/KEY: misc_feature
- 45 (B) LOCATION 1...156
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:
- Met Arg Asp Phe Asn Asn Ile Gln Ile Thr Arg Leu Lys Val Arg Gln 50

Asn Ala Val Phe Glu Lys Leu Asp Leu Glu Phe Lys Asp Gly Leu Ser

Ala Ile Ser Gly Ala Ser Gly Val Gly Lys Ser Val Leu Ile Ala Ser

Leu Leu Gly Ala Phe Gly Leu Lys Glu Ser Asn Ala Ser Asn Ile Glu

Val Glu Leu Ile Ala Pro Phe Leu Asp Thr Glu Glu Tyr Gly Ile Phe 70 Arg Glu Asp Glu His Glu Pro Leu Val Ile Ser Val Ile Lys Lys Glu 90 Lys Thr Arg Tyr Phe Leu Asn Gln Thr Ser Leu Ser Lys Asn Thr Leu 105 Lys Ala Leu Leu Lys Gly Leu Ile Lys Arg Leu Ser Asn Asp Arg Phe 120 125 Ser Gln Asn Glu Leu Asn Asp Ile Leu Met Leu Ser Leu Leu Asp Gly 135 140 Tyr Ile Gln Asn Lys Asn Arg Arg Leu Ala Pro Phe 150 15 (2) INFORMATION FOR SEQ ID NO:104: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 118 amino acids (B) TYPE: amino acid 20 (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: YES 25 (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: 30 (A) NAME/KEY: misc feature (B) LOCATION 1...118 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:104: Val Met Leu Met Ala Ile Phe Thr Pro Tyr Ile Leu Ile Leu Lys Met Met Lys Lys Ser Met Ser Leu Phe Ala Asn Met Gly Leu Glu Gln Ile Phe Cys Asn Arg Asp Ile Lys Asp Leu Asn Asp Phe Val Phe Gly Ile 40 Glu Val Gly Leu Asp Ser Asn Ala Arg Lys Asn Arg Ser Arg Lys Ala 55 Met Glu Asn His Leu Ile Gly Leu Phe Val Gln Ala Gln Leu Asn Phe 70 Lys Glu Gln Val Asp Ile Arg Glu Phe Glu Asp Leu Arg Gln Ala Phe 90 Gly Asn Asp Thr Lys Lys Phe Asp Phe Val Ile Phe Ser Lys Glu Lys 100 105 Thr Tyr Phe His Arg Ser 50 115 (2) INFORMATION FOR SEQ ID NO:105: (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 355 amino acids

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(B) TYPE: amino acid(D) TOPOLOGY: linear
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(ii) MOLECULE TYPE: protein

5

(iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

10

(ix) FEATURE:

(A) NAME/KEY: misc_feature

(B) LOCATION 1...355

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

Met Asn Ile Lys Ile Leu Lys Ile Leu Val Gly Gly Leu Phe Phe Leu Ser Leu Asn Ala His Leu Trp Gly Lys Gln Asp Asn Ser Phe Leu Gly 20 Ile Gly Glu Arg Ala Tyr Lys Ser Gly Asn Tyr Ser Lys Ala Ala Ser 40 Tyr Phe Lys Lys Ala Cys Asn Asp Gly Val Ser Glu Gly Cys Thr Gln 55 25 Leu Gly Ile Ile Tyr Glu Asn Gly Gln Gly Thr Arg Ile Asp Tyr Lys Lys Ala Leu Glu Tyr Tyr Lys Thr Ala Cys Gln Ala Asp Asp Arg Glu 90 Gly Cys Phe Gly Leu Gly Gly Leu Tyr Asp Glu Gly Leu Gly Thr Ala 30 100 Gln Asn Tyr Gln Glu Ala Ile Asp Ala Tyr Ala Lys Ala Cys Val Leu 120 Lys His Pro Glu Ser Cys Tyr Asn Leu Gly Ile Ile Tyr Asp Arg Lys 135 Ile Lys Gly Asn Ala Ala Gln Ala Val Thr Tyr Tyr Gln Lys Ser Cys Asn Phe Asp Met Ala Lys Gly Cys Tyr Ile Leu Gly Thr Ala Tyr Glu Lys Gly Phe Leu Glu Val Lys Gln Ser Asn His Lys Ala Val Ile Tyr 40 Tyr Leu Lys Ala Cys Arg Leu Asn Glu Gly Gln Ala Cys Arg Ala Leu 200 Gly Ser Leu Phe Glu Asn Gly Asp Ala Gly Leu Asp Glu Asp Phe Glu 215 Val Ala Phe Asp Tyr Leu Gln Lys Ala Cys Ala Leu Asn Asn Ser Gly 45 235 Gly Cys Ala Ser Leu Gly Ser Met Tyr Met Leu Gly Arg Tyr Val Lys 245 250 Lys Asp Pro Gln Lys Ala Phe Asn Tyr Phe Lys Gln Ala Cys Asp Met 50 265 Gly Ser Ala Val Ser Cys Ser Arg Met Gly Phe Met Tyr Ser Gln Gly Asp Thr Val Ser Lys Asp Leu Arg Lys Ala Leu Asp Asn Tyr Glu Arg 295 Gly Cys Asp Met Gly Asp Glu Val Gly Cys Phe Ala Leu Ala Gly Met

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310 Tyr Tyr Asn Met Lys Asp Lys Glu Asn Ala Ile Met Ile Tyr Asp Lys 330 325 Gly Cys Lys Leu Gly Met Lys Gln Ala Cys Glu Asn Leu Thr Lys Leu Arg Gly Tyr 355 (2) INFORMATION FOR SEQ ID NO:106: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 193 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear 15 (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: YES 20 (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc feature 25 (B) LOCATION 1...193 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:106: Met Lys Glu Lys Asn Phe Trp Pro Leu Gly Ile Met Ser Val Leu Ile 30 10 Phe Gly Leu Gly Ile Val Val Phe Leu Val Val Phe Ala Leu Lys Asn Ser Pro Lys Asn Asp Leu Val Tyr Phe Lys Gly His Asn Glu Val Asp 40 35 Leu Asn Phe Asn Ala Met Leu Lys Thr Tyr Glu Asn Phe Lys Ser Asn 55 Tyr Arg Phe Ser Val Gly Leu Lys Pro Leu Thr Glu Ser Pro Lys Thr 70 75 Pro Ile Leu Pro Tyr Phe Ser Lys Gly Thr His Gly Asp Lys Lys Ile 40 85 90 Gln Glu Asn Leu Leu Asn Asn Ala Leu Ile Leu Glu Lys Ser Asn Thr 105 Leu Tyr Ala Gln Leu Gln Pro Leu Lys Pro Ala Leu Asp Ser Pro Asn 120 45 Ile Gln Val Tyr Leu Ala Phe Tyr Pro Ser Gln Ser Gln Pro Arg Leu 135 140 Leu Gly Thr Leu Asp Cys Lys Asn Ala Cys Glu Pro Leu Lys Phe Asp 150 155 Leu Leu Glu Gly Asp Lys Val Gly Arg Tyr Lys Ile Leu Phe Lys Phe 50 165 _ 170 Val Phe Lys Asn Lys Glu Glu Leu Ile Leu Glu Gln Leu Ala Phe Phe 180 185 Lys

```
(2) INFORMATION FOR SEQ ID NO:107:
```

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 289 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- 10 (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

- 15 (ix) FEATURE:
  - (A) NAME/KEY: misc_feature
  - (B) LOCATION 1...289
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:107: 20

Leu Gly Ile Asn Met Cys Ser Lys Lys Ile Arg Asn Leu Ile Leu Cys

10

Phe Gly Phe Ile Leu Ser Leu Cys Ala Glu Glu Asn Ile Thr Lys Glu 25

Asn Met Thr Glu Thr Asn Thr Thr Glu Glu Asn Thr Pro Lys Asp Ala 25 40

Pro Ile Leu Leu Glu Glu Lys Arg Ala Gln Thr Leu Glu Leu Lys Glu 55

Glu Asn Glu Val Ala Lys Lys Ile Asp Glu Lys Ser Leu Leu Glu Glu 30

Ile His Lys Lys Lys Arg Gln Leu Tyr Met Leu Lys Gly Glu Leu His 85

Glu Lys Asn Glu Ser Ile Leu Phe Gln Gln Met Ala Lys Asn Lys Ser 100 105

Gly Phe Phe Ile Gly Val Ile Leu Gly Asp Ile Gly Ile Asn Ala Asn 120

Pro Tyr Glu Lys Phe Glu Leu Leu Ser Asn Ile Gln Ala Ser Pro Leu 135

Leu Tyr Gly Leu Arg Ser Gly Tyr Gln Lys Tyr Phe Ala Asn Gly Ile 40

Ser Ala Leu Arg Phe Tyr Gly Glu Tyr Leu Gly Gly Ala Met Lys Gly 170

Phe Lys Ser Asp Ser Leu Ala Ser Tyr Gln Thr Ala Ser Leu Asn Ile 180 185

Asp Leu Leu Met Asp Lys Pro Ile Asp Lys Glu Lys Arg Phe Ala Leu 200

Gly Ile Phe Gly Gly Val Gly Val Gly Trp Asn Gly Met Tyr Gln Asn 215 220

Leu Lys Glu Ile Arg Gly Tyr Ser Gln Pro Asn Ala Phe Gly Leu Val 50 230 235

Leu Asn Leu Gly Val Ser Met Thr Leu Asn Leu Lys His Arg Phe Glu 245 250

Leu Ala Leu Lys Met Pro Pro Leu Lys Glu Thr Ser Gln Thr Phe Leu 260 265

Tyr Tyr Phe Lys Ser Thr Asn Ile Tyr Tyr Ile Ser Tyr Asn Tyr Leu

- 181 -

275 280 285 Leu 5 (2) INFORMATION FOR SEQ ID NO:108: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 668 amino acids (B) TYPE: amino acid 10 (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: YES 15 (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: 20 (A) NAME/KEY: misc_feature (B) LOCATION 1...668 (xi) SEQUENCE DESCRIPTION: SEO ID NO:108: Met Arg Lys Leu Phe Ile Pro Leu Leu Phe Ser Ala Leu Glu Ala 10 Asn Glu Lys Asn Gly Phe Phe Ile Glu Ala Gly Phe Glu Thr Gly Leu 25 Leu Glu Gly Thr Gln Thr Gln Glu Lys Arg His Thr Thr Thr Lys Asn 30 40 Thr Tyr Ala Thr Tyr Asn Tyr Leu Pro Thr Asp Thr Ile Leu Lys Arg Ala Ala Asn Leu Phe Thr Asn Ala Glu Ala Ile Ser Lys Leu Lys Phe Ser Ser Leu Ser Pro Val Arg Val Leu Tyr Met Tyr Asn Gly Gln Leu 90 Thr Ile Glu Asn Phe Leu Pro Tyr Asn Leu Asn Asn Val Lys Leu Ser 105 Phe Thr Asp Ala Gln Gly Asn Thr Ile Asp Leu Gly Val Ile Glu Thr 40 120 Ile Pro Lys His Ser Lys Ile Val Leu Pro Gly Glu Ala Phe Asp Ser 135 Leu Lys Glu Ala Phe Asp Lys Ile Asp Pro Tyr Thr Leu Phe Leu Pro 150 155 45 Lys Phe Glu Ala Thr Ser Thr Ser Ile Ser Asp Thr Asn Thr Gln Arg 165 170 Val Phe Glu Thr Leu Asn Asn Ile Lys Thr Asn Leu Ile Met Lys Tyr 185 Ser Asn Glu Asn Pro Asn Asn Phe Asn Thr Cys Pro Tyr Asn Asn Asn 50 200

Gly Asn Thr Lys Asn Asp Cys Trp Gln Asn Phe Thr Pro Gln Thr Ala

Glu Glu Phe Thr Asn Leu Met Leu Asn Met Ile Ala Val Leu Asp Ser

Gln Ser Trp Gly Asp Ala Ile Leu Asn Ala Pro Phe Glu Phe Thr Asn

235

215

(2) INFORMATION FOR SEQ ID NO:109:

		٠,			245	;				250	)				255	
	Ser	Se	r Thi	: Asp	Суз	Asp	Ser	Asp	Pro	Ser	Lvs	Cvs	. Val	Δgr	Dro	Gly
				260	) -	-			265	;	. <i></i> y.	, cy.	, va.	270		, GIA
	Val	. Ası	a Gly	/ Arg	, Val	Asp	Thr	Lys	Val	Ast	Glr	Glr	ቸህ ነ	. Tle	, T.e.:	Asn
5			275	•				280	}				285	:		
	Lys	Gli	a Gly	/ Ile	: Ile	Asn	Asr	. Phe	Arg	Lvs	Lvs	Ile	Glu	lle	Agr	Ala
		290	J				295	5				300	1			
	Val	. Val	l Leu	Lys	Asn	Ser	Gly	⁄ Val	.Val	Gly	Leu	Ala	Asn	Glv	Tvr	Gly
10	305	,				310					315					320
10	Asn	Ası	Gly	Glu Glu	Tyr	Gly	Thr	Leu	Gly	Val	Glu	Ala	Tyr	Ala	Leu	Asp
					325					330	1.				335	
	Pro	Lys	Lys	Leu	Phe	Gly	Asn	ı Asp	Leu	Lys	Thr	Ile	Asn	Leu	Glu	Asp
				340					345					350		
15	ren	Arc	J Thr	ile	Leu	His	Glu	Phe	Ser	His	Thr	Lys	Gly	Tyr	Gly	His
13			333	•				360					365			
	ASII	370	ASI	Met	Thr	Tyr	GIn	Arg	Val	Pro	Val	Thr	Lys	Asp	Gly	Gln
	Va I	-		7.00	Com	3	375		_			380				
	385	OIU	Lys	Asp	ser	390	GIY	гуs	Pro	Lys			Asp	Gly	Leu	Pro
20			. Val	Cve	Ser				<b>~1</b>		395		_			400
	-1-		Val	Cys	405	пец	TYL	GIY	GIY	ser	Asn	Gln	Pro	Ala		Pro
	Ser	Asn	Tyr	Pro		Ser	Tle	ጥረም	ui.	410	0	77-	•		415	
			•	420				- 7 -	425	ASII	cys	ALA	Asp		Pro	Ala
	Gly	Phe	Leu	Gly	Val	Thr	Ala	Ala	Val	Trr	Gln	Gln	Lou	430	7	G1-
25			435	-				440		P	GIII	GIII	445	TIE	ASII	GIN
	Asn	Ala	Leu	Pro	Ile	Asn	Tyr	Ala	Asn	Leu	Glv	Ser	GJD	Thr	λen	Tree.
		350					455					460				
	Asn	Leu	Asn	Ala	Ser	Leu	Asn	Thr	Gln	Asp	Leu	Ala	Asn	Ser	Met	Leu
20	403					470					475					480
30	Ser	Thr	Ile	Gln	Lys	Thr	Phe	Val	Thr	Ser	Ser	Val	Thr	Asn	His	His
					485					490					495	
	Pne	ser	Asn	Ala	Ser	Gln	Ser	Phe	Arg	Ser	Pro	Ile	Leu	Gly	Val	Asn
				500					505					510		
35	ALG	nys	Ile 515	GIY	Tyr	GIn	Asn	Tyr	Phe	Asn	Asp	Phe	Ile	Gly	Leu	Ala
J J	Tvr	ጥህም		Tlo	T10	T		520	_		•		525			
	-1-	530	Gly	116	116	гÀг	535	Asn	Tyr	Ala	Lys		Val	Asn	Gln	Lys
	Val		Gln	Leu	Ser	<b>ጥ</b> ህን	235 G1v	Gl v	<b>~1</b>	T1 -	3	540	_	_	_	
	545					550	GLY	GLY	GIŞ	ire		Leu	Leu	Leu	Asp	
40	Ile	Thr	Thr	Tyr			Lvs	Asn	Ser	Dro	555		T1.	<b>~1</b>	m>	560
					202					570					676	
	Arg	Asn	Phe	Ser	Ser	Ser	Phe	Glv	Ile	Phe	Glv	Glv	Len	λνα	2/2: Clu	T 011
				300					585					590	-	
	Tyr	Asn	Ser	Tyr	Tyr	Val	Leu	Asn	Lys	Val	Lvs	Glv	Ser	Glv	Δsn	T.e.r
45			222					600					605			
	Asp	Val	Ala	Thr	Gly	Leu	Asn	Tyr	Arg	Tyr	Lys	His	Ser	Lvs	Tvr	Ser
		010					615					620				
	Val	Gly	Ile	Ser	Ile	Pro	Leu	Ile	Gln	Arg	Lys	Ala	Ser	Val	Val	Ser
50	025					630					635		•			640
JU	ser	σтλ	Gly	Asp	Tyr	Thr	Asn	Ser	Phe	Val	Phe	Asn	Glu	Gly	Ala	Ser
					045					650					655	
	mis .	FIIE	Lys	val	rue	rne	Asn			Trp	Val	Phe				
				660					665	•						

	·
_	<ul><li>(i) SEQUENCE CHARACTERISTICS:</li><li>(A) LENGTH: 63 amino acids</li><li>(B) TYPE: amino acid</li></ul>
5	(D) TOPOLOGY: linear
	(ii) MOLECULE TYPE: protein
10	(iii) HYPOTHETICAL: YES
	(vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori
15	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 163</pre>
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:
20	Met Asn Thr Glu Ile Leu Thr Ile Met Leu Val Val Ser Val Leu Met  1 5 10 15
	Gly Leu Val Gly Leu Ile Ala Phe Leu Trp Gly Val Lys Ser Gly Gln 20 25 30
25	Phe Asp Asp Glu Lys Arg Met Leu Glu Ser Val Leu Tyr Asp Ser Ala 35 40 45
	Ser Asp Leu Asn Glu Ala Ile Leu Gln Glu Lys Arg Gln Lys Asn 50 55 60
30	(2) INFORMATION FOR SEQ ID NO:110:
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 406 amino acids  (B) TYPE: amino acid
35	(D) TOPOLOGY: linear
	(ii) MOLECULE TYPE: protein
۱۸.	(iii) HYPOTHETICAL: YES
10	(vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori
15	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 1406</pre>
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:
0	Met Val Phe Phe His Lys Lys Ile Ile Leu Asn Phe Ile Tyr Ser Leu  1 5 10 15
_	Met Val Ala Phe Leu Phe His Leu Ser Tyr Gly Val Leu Leu Lys Ala
	Asp Gly Met Ala Lys Lys Gln Thr Leu Leu Val Gly Glu Arg Leu Val
5	Trp Asp Lys Leu Thr Leu Leu Gly Phe Leu Glu Lys Asn His Ile Pro

		50	_	_			55					60					
	Gin	Lys	Leu	Tyr	Tyr	Asn	Leu	Ser	Ser	Gln	Asp	Lys	Glu	Leu	Ser	Ala	
	65					70					75					80	
	Glu	Ile	Gln	Ser	Asn	Val	Thr	Tyr	Tyr	Thr	Leu	Arg	Asp	Ala	Asn	Asn	
5					85					90					95		
	Thr	Leu	Ile	Gln	Ala	Leu	Ile	Pro	Ile	Ser	Gln	Asp	Leu	Gln	Ile	His	
				100					105					110			
	Ile	Tyr	Lys	Lys	Gly	Glu	Asp	Tvr			Asn	Dhe	Tla	Dro	Tla	17-1	
		_	115	-				120			·	FIIC	125	FIO	116	vai	
10	Phe	Thr	Ara	Lvs	Glu	Arg	Thr			Lau	P.~~	T 000	41-	mb	C	D	
		130				3	135	Leu	neu	neu	Ser		GIII	THE	ser	Pro	
	ጥህጉ			Tle	17a 1	Lys			7		<b>D</b>	140	_		_		
	145	· · · ·			Val	150	MIG	1111	ASII	Asp		ьeu	Leu	Ala	Asn		
			λαη	7 l -	Т. т.		<b>.</b>	<b>^</b>		_	155					160	
15	пец	FIEL	Wali	nia	171	Lys	гуз	ser	vai			Lys	Arg	Leu		Lys	
13		7	7	<b>T</b> 1 -	165				_	170					175		
	ASII	Asp	гÃ2	TTE	ATA	Ile	Val	Tyr		Arg	Asp	Tyr	Arg	Val	Gly	Gln	
				180					185					190			
	Ala	Pne	GIY	GIn	Pro	Thr	Ile		Met	Ala	Met	Val	Ser	Ser	Arg	Leu	
20	•		195					200					205				
20	His	Gln	Tyr	Tyr	Leu	Phe	Ser	His	Ser	Asn	Gly	Arg	Tyr	Tyr	Asp	Ser	
		210					215					220					
	Lys	Ala	Gln	Glu	Val	Ala	Gly	Phe	Leu	Leu	Glu	Thr	Pro	Val	Lys	Tyr	
	225					230					235					240	
	Thr	Arg	Ile	Ser	Ser	Pro	Phe	Ser	Tyr	Gly	Arg	Phe	His	Pro	Val	Leu	
25					245					250		•			255		
	Lys	Val	Lys	Arg	Pro	His	Tyr	Gly	Val	Asp	Tyr	Ala	Ala	Lvs	His	Glv	
				260					265					270			
	Ser	Leu	Ile	His	Ser	Ala	Ser	Asp	Gly	Arg	Val	Glv	Phe	Ile	Glv	Val	
			275					280					285				
30	Lys	Ala	Gly	Tyr	Gly	Lys	Val	Val	Glu	Ile	His	Leu	Asn	Glu	T.e.11	Ara	
		290				-	295					300				g	
	Leu	Val	Tyr	Ala	His	Met	Ser	Ala	Phe	Δla	Δsn	Glv	T.em	Lare	Lize	C1.	
	305					310					315	u_j.	<u> </u>	Lys	Lys	320	
	Ser	Phe	Val	Lys	Lvs	Gly	Gln	Tle	T}e	Glv	Ara	17-1	Glar.	co~	mb	220	
35				•	325					330	AT 9	vai	GLY	ser		GIY	
	Leu	Ser	Thr	Glv	Pro	His	T.em	Hic	Dhe	Glar	17 a 1	TT	<b>7</b>	*	335		
				340					345	GIY	val	TÄT	ьys		ser	Arg	
	Pro	Ile			Len	Gly	т	T1.0		mbaa	77.	<b>*</b>		350	_		
			355			O _T y	- y -	360	Arg	THE	ALA	гÀа		гуѕ	Leu	His	
40	Glv	Tage		λνα	Glu	37-3	Dh-		<b>~</b> 7.	-			365				
	027	370	0111	nig.	GIU	Val	PHE 375	Leu	GIU	гÀа	Ala		Tyr	Ser	Lys	Gln	
·.	Lare			G1	T. 011		375	m).	<b></b> ·	_		380					
	385	Teu	GI U	GIU	Ten	Phe	ьys	Thr	Hls			Glu	Lys	Asn	Ser	Phe	
		ī	T 0	<b>a</b> 1	<b>01</b>	390					395					400	
45	TAL	neu	Leu	GIU	_	ьиe											
73					405		•										
										*.							

# (2) INFORMATION FOR SEQ ID NO:111:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 296 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

```
(iii) HYPOTHETICAL: YES
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
               (B) LOCATION 1...296
10
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:
     Leu Phe Leu Val Lys Lys Ile Gly Val Val Ile Met Ile Leu Val Cys
     Phe Leu Ala Cys Ser Gln Glu Ser Phe Ile Lys Met Gln Lys Lys Ala
15
                                     25
    Gln Glu Gln Glu Asn Asp Gly Ser Lys Arg Pro Ser Tyr Val Asp Ser
     Asp Tyr Glu Val Phe Ser Glu Thr Ile Phe Leu Gln Asn Met Val Tyr
20
     Gln Pro Ile Glu Glu Arg Asn Ala Phe Phe Gln Leu Thr Lys Asp Glu
                                             75
    Asp Asn Ser Phe Asn Pro Glu Asn Ser Val Ile Leu Leu Asn Glu Pro
                     85
                                         90
     Ser Asp Asn Ser Glu Lys Asn Leu Leu Ser Tyr Pro Asn Asp Pro Asn
25
                                     105
     Asn Asn Glu Asp Asn Ala Asn Asn Ser Gln Lys Asn Pro Phe Leu Tyr
                                120
     Lys Pro Lys Arg Lys Thr Lys Asn Pro Lys Leu Ile Glu Tyr Ser Gln
                             135
30
     Gln Asp Phe Tyr Pro Leu Lys Asn Gly Asp Ile Ile Met Ser Lys Glu
                         150 *
                                             155
    Gly Asp Gln Trp Leu Ile Glu Ile Gln Ser Lys Ala Leu Lys Arg Phe
                     165
                                         170
    Leu Lys Asp Gln Asn Asp Lys Asp Arg Gln Ile Gln Thr Phe Thr Phe
35
                                     185
    Asn Asp Thr Lys Thr Gln Ile Ala Gln Ile Lys Gly Lys Ile Ser Ser
                                 200
    Tyr Val Tyr Thr Thr Asn Asn Gly Ser Leu Ser Leu Arg Pro Phe Tyr
                                                 220
40
    Glu Ser Phe Leu Leu Glu Lys Lys Ser Asp Asn Val Tyr Thr Ile Glu
                        230
                                           235
    Asn Lys Ala Leu Asp Thr Met Glu Ile Ser Lys Cys Gln Met Val Leu
                    245
                                         250
    Lys Lys His Ser Thr Asp Lys Leu Asp Ser Gln His Lys Ala Ile Ser
45
                           . 265
    Ile Asp Leu Asp Phe Lys Lys Glu Arg Phe Lys Ser Asp Thr Glu Leu
    Phe Leu Glu Cys Leu Lys Glu Ser
        290
```

- (2) INFORMATION FOR SEQ ID NO:112:
  - (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 248 amino acids(B) TYPE: amino acid

```
(D) TOPOLOGY: linear
```

- (ii) MOLECULE TYPE: protein
- 5 (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

- 10 (ix) FEATURE:
  - (A) NAME/KEY: misc_feature
  - (B) LOCATION 1...248
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:112:0
- 15 Val Ser Tyr Asp Asn Thr Asp Asp Tyr Tyr Phe Pro Arg Asn Gly Val

Ile Phe Ser Ser Tyr Ala Thr Met Ser Gly Leu Pro Ser Ser Gly Thr

Leu Asn Ser Trp Asn Gly Leu Gly Gly Asn Val Arg Asn Thr Lys Val 20

Tyr Gly Lys Phe Ala Ala Tyr His His Leu Gln Lys Tyr Leu Leu Ile

Asp Leu Ile Ala Arg Phe Lys Thr Gln Gly Gly Tyr Ile Phe Arg Tyr 25 70 75

Asn Thr Asp Asp Tyr Leu Pro Leu Asn Ser Thr Phe Tyr Met Gly Gly 90

Val Thr Thr Val Arg Gly Phe Arg Asn Gly Ser Ile Thr Pro Lys Asp 100 105

Glu Phe Gly Leu Trp Leu Gly Gly Asp Gly Ile Phe Thr Ala Ser Thr 30 120

Glu Leu Ser Tyr Gly Val Leu Lys Ala Ala Lys Met Arg Leu Ala Trp 135

Phe Phe Asp Phe Gly Phe Leu Thr Phe Lys Thr Pro Thr Arg Gly Ser 35 150 155

Phe Phe Tyr Asn Ala Pro Thr Thr Thr Ala Asn Phe Lys Asp Tyr Gly 165 170

Val Val Gly Ala Gly Phe Glu Arg Ala Thr Trp Arg Ala Ser Thr Gly 185

Leu Gln Ile Glu Trp Ile Ser Pro Met Gly Pro Leu Val Leu Ile Phe 200

Pro Ile Ala Phe Phe Asn Gln Trp Gly Asp Gly Asn Gly Lys Lys Cys 215 220

Lys Gly Leu Cys Phe Asn Pro Asn Met Asn Asp Tyr Thr Gln His Phe 45 230 235

Glu Phe Ser Met Gly Thr Arg Phe

(2) INFORMATION FOR SEQ ID NO:113:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 335 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear

35

40

45

50

55

Leu Phe Ser Ile Ala

Leu Glu Gln Ala Arg 30 Leu Gln Lys Phe Ala

Leu Asp Glu Leu Leu

Ala Arg Ala Tyr Ser

Lys Gly Leu Leu Asn

Leu Asp Leu Leu Ala 110 Thr Lys Asp Thr Val

95

45

125

15

								•	- 1	87 -	•
		(ii	) MO	LECU	LE T	YPE:	pro	tein			
		(iii	) HY	POTH	ETIC	AL:	YES				
5		(vi				OURC:		icob	acte	r py:	lori
•		(ix	) FE			KEY:	mis	c_fe	atur	e	
10			(1	B) L	OCAT:	ION :	1;	335			
		(xi	) SE	QUEN	CE D	ESCR:	IPŢI(	ЭИ:	SEQ :	ID N	0;:11:
15	Val 1	Gln	His	Phe	Asn 5	Phe	Leu	Tyr	Lys	Asp 10	Ser
	Leu	Phe	Thr	Phe 20	Ile	Ile	Ala	Leu	Val 25	Ile	Leu
٠	Ala	Tyr	Phe 35	Thr	Arg	Lys	Arg	Asn 40	Lys	Lys	Phe
20	Gln	Asn 50	Gln	Asn	Ala	Tyr	Ala 55	Ser	Ser	Glu	Asn
	Lys 65	His	Ala	Lys	Ile	Ser 70	Ser	Leu	Met	Phe	Leu 75
25	Lys	Ala	Asp	Val	Glu 85	Met	Ser	Ile	Glu	Ile 90	Leu
	Arg	Pro	Leu	Lys 100	Asp	Glu	Glu	Lys	Ile 105	Ala	Val
	Lys		Tyr 115	Phe	Ser	Val	Gly	Tyr 120	Leu	Gln	Lys

120

135

215

295

150

230

310

165

245

. .

325

Lys Glu Ile Leu Arg Phe Ser Pro Arg Asn Val Glu Ala Leu Leu Lys

Leu Leu His Ala Tyr Glu Leu Glu Lys Asp Tyr Ser Lys Ala Leu Glu

Thr Leu Glu Cys Leu Glu Glu Leu Glu Val Pro Lys Ile Glu Thr Ile

Lys Asn Tyr Leu Tyr Leu Met His Leu Ile Glu Asn Lys Glu Asp Ala 185 Ala Lys Ile Leu His Val Ser Lys Ala Ser Leu Asp Leu Lys Lys Ile 200

Ala Leu Asn His Leu Lys Ser His Asp Glu Asn Leu Phe Trp Gln Glu

Ile Asp Thr Thr Glu Arg Leu Glu Asn Val Ile Asp Leu Leu Trp Asp

Met Asn Ile Pro Ala Phe Ile Leu Glu Lys His Ala Leu Leu Gln Asp

Ile Ala Arg Ser Gln Gly Leu Leu Leu Asp His Lys Pro Cys Gln Ile 265 Phe Glu Leu Glu Val Leu Arg Ala Leu Leu His Ser Pro Ile Lys Ala 280

Ser Leu Thr Phe Glu Tyr Arg Cys Lys His Cys Lys Gln Ile Phe Pro

Phe Glu Ser His Arg Cys Pro Val Cys Tyr Gln Leu Ala Phe Met Asp

Met Val Leu Lys Ile Ser Lys Lys Thr His Ala Met Gly Val Asp

. 155

235

315

300

170

250

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(2) INFORMATION FOR SEQ ID NO:114:
           (i) SEQUENCE CHARACTERISTICS:
 5
                (A) LENGTH: 413 amino acids
                (B) TYPE: amino acid
                (D) TOPOLOGY: linear
         (ii) MOLECULE TYPE: protein
10
         (iii) HYPOTHETICAL: YES
         (vi) ORIGINAL SOURCE:
                (A) ORGANISM: Helicobacter pylori
15
         (ix) FEATURE:
                (A) NAME/KEY: misc_feature
                (B) LOCATION 1...413
20
         (xi) SEQUENCE DESCRIPTION: SEO ID NO:114:
     Met Arg Lys Ile Phe Ser Tyr Ile Ser Lys Val Leu Leu Phe Ile Gly
                                          10
     Val Val Tyr Ala Glu Pro Asp Ser Lys Val Glu Ala Leu Glu Gly Arg
25
                                      25
     Lys Gln Glu Ser Ser Leu Asp Lys Lys Ile Arg Gln Glu Leu Lys Ser
                                 40
     Lys Glu Leu Lys Asn Lys Glu Leu Lys Asn Lys Asp Leu Lys Asn Lys
                             55
30
     Glu Glu Lys Lys Glu Thr Lys Ala Lys Arg Lys Pro Arg Ala Glu Val
                         70
                                             75
     His His Gly Asp Ala Lys Asn Pro Thr Pro Lys Ile Thr Pro Pro Lys
     Ile Lys Gly Ser Ser Lys Gly Val Gln Asn Gln Gly Val Gln Asn Asn
35
                                      105
     Ala Pro Lys Pro Glu Glu Lys Asp Thr Thr Pro Gln Ala Thr Glu Lys
                                 120
     Asn Lys Glu Thr Ser Pro Ser Ser Gln Phe Asn Ser Ile Phe Gly Asn
                             135
    Pro Asn Asn Ala Thr Asn Asn Thr Leu Glu Asp Lys Val Val Gly Gly
40
                         150
                                             155
     Ile Ser Leu Leu Val Asn Gly Ser Pro Ile Thr Leu Tyr Gln Ile Gln
                                         170
     Glu Glu Gln Glu Lys Ser Lys Val Ser Lys Ala Gln Ala Arg Asp Arg
45
                                     185
    Leu Ile Ala Glu Arg Ile Lys Asn Gln Glu Ile Glu Arg Leu Lys Ile
                                 200
     His Val Asp Asp Asp Lys Leu Asp Gln Glu Met Ala Met Met Ala Gln
                             215
50
    Gln Gln Gly Met Asp Leu Asp His Phe Lys Gln Met Leu Met Ala Glu
```

55

Gly His Tyr Lys Leu Tyr Arg Asp Gln Leu Lys Glu His Leu Glu Met

Gln Glu Leu Leu Arg Asn Ile Leu Leu Thr Asn Val Asp Thr Ser Ser

265

235

	Glu	Thr	Lys 275	Met	Arg	Glu	Tyr	Tyr 280	Asn	Lys	His	Lys	Glu 285		Phe	Ser
	Ile	Pro 290	Thr	Glu	Ile	Glu	Thr 295	Val	Arg	Tyr	Thr	Ser 300			Gln	Glu
5	Asp 305		Glu	Arg	Ala	Met 310	Ala	Asp	Pro	Asn	Leu 315	Glu	Val	Pro	Gly	Val
	Ser	Lys	Ala	Asn	Glu 325		Iļe	Glu	Met	Lys 330	Thr	Leu	Asn	Pro	Gln 335	
10	Ala	Gln	Val	Phe 340		Ser	His	Glu	Gln 345	Gly	Ser	Phe	Thr	Pro 350		Met
	Asn	Gly	Gly 355	Gly	Gly	Gln	Phe	Ile 360	Thr	Phe	Tyr	Ile	Lys 365	Glu	Lys	Arg
٠	Gly	Lys 370	Asn	Glu	Val	Ser	Phe 375		Gln	Ala	Lys	Gln 380	Phe	Ile	Ala	Gln
15	Lys 385		Val	Glu	Glu	Ser 390	Lys	Asp	Lys	Ile	Leu 395	Glu	Glu	His		Glu 400
-	Lys	Leu	Arg	Val	Lys 405	Ser	Arg	Ile	Val	Met 410		Arg	Glu	•		
20	(2)	INFO	ORMA'	rion	FOR	SEQ	ID I	NO:1	15:							
		(i)	) SEC	QUEN	CE CI	HARA	CTER:	ISTIC	CS:							
			(2	A) LI	ENGTI	H: 18	86 ar	mino		ds						
25			. (1	) T(	OPOL	OGY:	line	ear								•
		(ii)	MO	LECUI	LE T	YPE:	pro	tein								
30		(iii)	HY	РОТНІ	ETIC	AL: Y	YES		•				•			
,0		(vi)				OURCI		icoba	acte	r py:	lori					
35		(ix)		ATURI		KEY:	mis	r fe:	2 <b>†</b> 11 <b>*</b> 1	<b>a</b>						
						CON 1		_	*CU1							
		(xi)	SEÇ	QUENC	CE DI	ESCRI	IPTIC	ON: S	SEQ :	ID NO	0:11	5:				
10	Met 1	Ile	Lys	Arg	Ile 5				Leu	Ser 10	Leu	Ser	Ala	Ser	Leu 15	Ala
	Leu	Ala	Gly	Glu 20	Val	Asn	Gly	Phe	Phe 25	Met	Gly	Ala	Gly	Tyr 30		Gln
15	Gly	Arg	Tyr 35	Gly	Pro	Tyr	Asn	Ser 40	Asn	Tyr	Ser	Asp	Trp 45	Arg	His	Gly
		Asp 50	Leu	Tyr	Gly	Leu	Asn 55	Phe	Lys	Leu	Gly	Phe 60	Val	Gly	Phe	Ala
	Asn 65	Lys	Trp	Phe	Gly	Ala 70	Arg	Val	Tyr	Gly	Phe		Asp	Trp	Phe	Asn 80
0	Thr	Ser	Gly	Thr	Glu 85	His	Thr	Lys	Thr	Asn 90		Leu	Thr	Tyr	Gly 95	
	Gly	Gly	Asp	Leu		Val	Asn		Ile	Pro	Leu	Asp	Lys	Phe		Leu

Gly Leu Ile Gly Gly Val Gln Leu Ala Gly Asn Thr Trp Met Phe Pro 115 120 125

```
- 190 -
     Tyr Asp Val Asn Gln Thr Arg Phe Gln Phe Leu Trp Asn Leu Gly Gly
                              135
     Arg Met Arg Val Gly Asp Arg Ser Ala Phe Glu Ala Gly Val Lys Phe
                                              155
     Pro Met Val Asn Gln Gly Ser Lys Asp Val Gly Leu Ile Arg Tyr Tyr
                      165
                                          170
     Ser Trp Tyr Val Asp Tyr Val Phe Thr Phe
                  180
10
      (2) INFORMATION FOR SEQ ID NO:116:
           (i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 242 amino acids
                (B) TYPE: amino acid
15
                (D) TOPOLOGY: linear
          (ii) MOLECULE TYPE: protein
         (iii) HYPOTHETICAL: YES
20
          (vi) ORIGINAL SOURCE:
                (A) ORGANISM: Helicobacter pylori
          (ix) FEATURE:
25
                (A) NAME/KEY: misc feature
                (B) LOCATION 1...242
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:116:
30
     Met Lys Lys Phe Phe Ser Gln Ser Leu Leu Ala Leu Ile Ile Ser Met
                                          10
     Asn Ala Val Ser Gly Met Asp Gly Asn Gly Val Phe Leu Gly Ala Gly
                                      25
     Tyr Leu Gln Gly Gln Ala Gln Met His Ala Asp Ile Asn Ser Gln Lys
                                  40
     Gln Ala Thr Asn Ala Thr Ile Lys Gly Phe Asp Ala Leu Leu Gly Tyr
                            - 55
```

35 Gln Phe Phe Phe Glu Lys His Phe Gly Leu Arg Leu Tyr Gly Phe Phe 70 40 Asp Tyr Ala His Ala Asn Ser Ile Lys Leu Lys Asn Pro Asn Tyr Asn Ser Glu Ala Ala Gln Val Ala Ser Gln Ile Leu Gly Lys Gln Glu Ile 105 Asn Arg Leu Thr Asn Ile Ala Asp Pro Arg Thr Phe Glu Pro Asn Met 120 Leu Thr Tyr Gly Gly Ala Met Asp Val Met Val Asn Val Ile Asn Asn 135 Gly Ile Met Ser Leu Gly Ala Phe Gly Gly Ile Gln Leu Ala Gly Asn 155 50 Ser Trp Leu Met Ala Thr Pro Ser Phe Glu Gly Ile Leu Val Glu Gln 170 Ala Leu Val Ser Lys Lys Ala Thr Ser Phe Gln Phe Leu Phe Asn Val

180 185 190 Gly Ala Arg Leu Arg Ile Leu Lys His Ser Ser Ile Glu Ala Gly Val

Lys Phe Pro Met Leu Lys Lys Asn Pro Tyr Ile Thr Ala Lys Asn Leu 210 215 220

Asp Ile Gly Phe Arg Arg Val Tyr Ser Trp Tyr Val Asn Tyr Val Phe 225 230 230 240

Thr Phe

#### (2) INFORMATION FOR SEQ ID NO:117:

- 10 (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 256 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- 15 (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES
- (vi) ORIGINAL SOURCE:
- 20 (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:
    - (A) NAME/KEY: misc_feature
    - (B) LOCATION 1...256
- 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:117:

.

Met Gly Tyr Ala Ser Lys Leu Ala Leu Lys Ile Cys Leu Val Gly Leu 1 5 10 15 30 Cys Leu Phe Ser Thr Leu Gly Ala Glu His Leu Glu Gln Lys Gly Asn

Cys Leu Phe Ser Thr Leu Gly Ala Glu His Leu Glu Gln Lys Gly Asn 20 25 30

Tyr Ile Tyr Lys Gly Glu Glu Ala Tyr Asn Asn Lys Glu Tyr Glu Arg
35 40 45

Ala Ala Ser Phe Tyr Lys Ser Ala Ile Lys Asn Gly Glu Ser Leu Ala 35 50 55 60

Tyr Ile Leu Leu Gly Ile Met Tyr Glu Asn Gly Arg Gly Val Pro Lys 65 70 75 80

Asp Tyr Lys Lys Ala Val Glu Tyr Phe Gln Lys Ala Val Asp Asn Asp 85 90 95

40 Ile Pro Arg Gly Tyr Asn Asn Leu Gly Val Met Tyr Lys Glu Gly Lys
100 105 110

Gly Val Pro Lys Asp Glu Lys Lys Ala Val Glu Tyr Phe Arg Ile Ala 115 120 125

Thr Glu Lys Gly Tyr Thr Asn Ala Tyr Ile Asn Leu Gly Ile Met Tyr 45 130 135 140

Met Glu Gly Arg Gly Val Pro Ser Asn Tyr Ala Lys Ala Thr Glu Cys 145 150 155 160

Phe Arg Lys Ala Met His Lys Gly Asn Val Glu Ala Tyr Ile Leu Leu

50 Gly Asp Ile Tyr Tyr Ser Gly Asn Asp Gln Leu Gly Ile Glu Pro Asp 180 185 190

Lys Asp Lys Ala Val Val Tyr Tyr Lys Met Ala Ala Asp Val Ser Ser
195 200 205

Ser Arg Ala Tyr Glu Gly Leu Ser Glu Ser Tyr Arg Tyr Gly Leu Gly 55 210 215 220

Val Glu Lys Asp Lys Lys Ala Glu Glu Tyr Met Gln Lys Ala Cys 230 235 Asp Phe Asp Ile Asp Lys Asn Cys Lys Lys Asn Thr Ser Ser Arg 250 5 (2) INFORMATION FOR SEQ ID NO:118: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 657 amino acids 10 (B) TYPE: amino acid (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein 15 (iii) HYPOTHETICAL: YES (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori 20 (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1...657 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:118: 25 Met Arg Lys Leu Phe Ile Pro Leu Leu Leu Phe Ser Ala Leu Glu Ala 10 Asn Glu Lys Asn Gly Phe Phe Ile Glu Ala Gly Phe Glu Thr Gly Leu 30 Leu Glu Gly Thr Gln Thr Gln Glu Lys Arg His Thr Thr Thr Lys Asn 40 Thr Tyr Ala Thr Tyr Asn Tyr Leu Pro Thr Asp Thr Ile Leu Lys Arg 55 Ala Ala Asn Leu Phe Thr Asn Ala Glu Ala Ile Ser Lys Leu Lys Phe 35 70 75 Ser Ser Leu Ser Pro Val Arg Val Leu Tyr Met Tyr Asn Gly Gln Leu 85 90 Thr Ile Glu Asn Phe Leu Pro Tyr Asn Leu Asn Asn Val Lys Leu Ser 105 40 Phe Thr Asp Ala Gln Gly Asn Val Ile Asp Leu Gly Val Ile Glu Thr 120 Ile Pro Lys His Ser Lys Ile Val Leu Pro Gly Glu Ala Phe Asp Ser 135 Leu Lys Ile Asp Pro Tyr Thr Leu Phe Leu Pro Lys Ile Glu Ala Thr 45 150 155 Ser Thr Ser Ile Ser Asp Ala Asn Thr Gln Arg Val Phe Glu Thr Leu 165 170 Asn Lys Ile Lys Thr Asn Leu Val Val Asn Tyr Arg Asn Glu Asn Lys 180 185 Phe Lys Asp His Glu Asn His Trp Glu Ala Phe Thr Pro Gln Thr Ala 200 Glu Glu Phe Thr Asn Leu Met Leu Asn Met Ile Ala Val Leu Asp Ser 215 220

Gln Ser Trp Gly Asp Ala Ile Leu Asn Ala Pro Phe Glu Phe Thr Asn

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	Ser	Pro	Thr	Asp	Cys 245	Asp	Asn	Asp	Pro	Ser 250	Lys	Суз	Val	Asn	Pro 255	Gly
	Thr	Asn	Gly	Leu 260	Val	Asn	Ser	Lys	Val 265	Asp	Gln	Lys	Tyr	Val 270	Leu	Asn
5	Lys	Gln	Asp 275	Ile	Val	Asn	Lys	Phe 280	Lys	Asn	Lys	Ala	Asp 285	Leu	Asp	Val
•	Ile	Val 290		Lys	Asp	Ser	Gly 295	Val	Val	Gly	Leu	Gly 300	Ser	Asp	Ile	Thr
10	Pro 305	Ser	Asn	Asn	Asp	Asp 310	Gly	Lys	His	Tyr	Gly 315	Gln	Leu	Gly	Val	Val 320
	Ala	Ser	Ala	Leu	Asp 325	Pro	Lys	Lys	Leu	Phe 330	Gly	Asp	Asn	Leu	Lys 335	Thr
				340			•		345					Ser 350		
15			355					360					365	Val		
		370					375					380		Pro		_
20	385	-	-			390			-		395	•	•	Gly		400
					405		•			410				His	415	
25				420					425					Val 430		
23			435					440				-	445	Asn		•
		450			_		455					460		Gln	_	
30	465					470					475			Arg		480
					485					490				Phe	495	
35				500			_		505	-			_	510 Tyr		
			515	÷			•	520					525	Gly		
		530					535				_	540	_	Ser		_
40	545					550					555			Ile		560
٠	_				565					570			_	Lys	575	
45	Gly	Ser	Gly	580 Asn	Leu	Asp	·Val	Ala	585 Thr	Gly	Leu	Asn	Tyr	590 Arg	Tyr	Lys
			595		ŧ			600					605	Gln		
	Ala	610 Ser	Val	Val	Ser	Ser	615 Gly	Gly	Asp	Tyr	Thr	620 Asn	Ser	Phe	Val	Phe .
50	625 Asn	Glu	Gly	Ala	Ser	630 His	Phe	Lys	Val	Phe	635 Phe	Asn	Tyr	Gly	Trp	640 Val
	Phe				645					650				•	655	

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(2) INFORMATION FOR SEQ ID NO:119:
```

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 167 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- 10 (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Helicobacter pylori
- 15 (ix) FEATURE:
  - (A) NAME/KEY: misc_feature
  - (B) LOCATION 1...167
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:119:
- 20 Met Lys Leu Val Ser Leu Ile Val Ala Leu Val Phe Cys Cys Phe Leu

10 Gly Ala Val Glu Leu Pro Gly Val Tyr Gln Thr Gln Glu Phe Leu Tyr

20 25

Met Lys Ser Ser Phe Val Glu Phe Phe Glu His Asn Gly Lys Phe Tyr

Ala Tyr Gly Ile Ser Asp Val Asp Gly Ser Lys Ala Lys Lys Asp Lys 55

Leu Asn Pro Asn Pro Lys Leu Arg Asn Arg Ser Asp Lys Gly Val Val 30 70

Phe Leu Ser Asp Leu Ile Lys Val Gly Glu Gln Ser Tyr Lys Gly Gly 90

Lys Ala Tyr Asn Phe Tyr Asp Gly Lys Thr Tyr His Val Arg Val Thr 105

Gln Asn Ser Asn Gly Asp Leu Glu Phe Thr Ser Ser Tyr Asp Lys Trp 35 120 125

Gly Tyr Val Gly Lys Thr Phe Thr Trp Lys Arg Leu Ser Asp Glu Glu

Ile Lys Asn Leu Lys Leu Lys Arg Phe Asn Leu Asp Glu Val Leu Lys 40 155 Thr Leu Lys Asp Ser Pro Ile 165

(2) INFORMATION FOR SEQ ID NO:120:

45

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 294 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein
- (iii) HYPOTHETICAL: YES
- 55 (vi) ORIGINAL SOURCE:

# (A) ORGANISM: Helicobacter pylori

#### (ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION 1...294

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:120:

				_												
10		Ser	Asn	Gln	Ala	Ser	His	Leu	Asp		Phe	Met	Asn	Ala	_	Asn
10	1	_	_	_,	5	_	_	_		10					15	
	Pro	Lys	Ser		Pne	Asp	Asn	Lys	_	Asn	Thr	Lys	Phe		Ala	Ile
	The se	Com	C1	20	C1	C1	17-1	~3	25	0	3	<b>-1</b> -	<b>a</b>	30	N	*
	1111	ser	35	пåя	GLY	Gly	vaı	40 .	rys	ser	AŞII	ite	ser	АТа	ASI	Leu
15	Ala	Tvr		Len	ጥህን	Lys	Lvs		Tvr	Lave	V=1	Glv		Dhe	) an	<b>Δ</b> 1 =
		50			-1-	_,_	55		1 -	Lys	Val	60	Val	1110	rsp	YT.
	Asp		Gly	Leu	Ala	Asn		Asp	Val	Ile	Phe		Val	Lvs	Thr	His
	65		-			70		•			75	2				80
	Lys	Asn	Ile	Leu	His	Ala	Leu	Lys	Gly	Glu	Ala	Lys	Leu	Gln	Glu	Ile
20					85					90					95	•
	Ile	Cys	Glu		Glu	Pro	Gly	Leu		Leu	Ile	Pro	Gly	Asp	Ser	Gly
				100		_	_		105	_				110		
	Glu	Glu		Leu	Lys	Tyr	Ile		Gly	Ala	Glu	Ala		Asp	Arg	Phe
25	1707	7	115	G3	a1	17-1	T	120		<b>T</b>	•		125			<b>.</b>
23	vai	130	GIU	GIU	GIY	Val	135	ser	ser	Leu	Asp	140	TTE	vai	TTE	Asp
	Thr		Ala	Glv	Tle	Gly		Thr	Thr	Gln	Δla		T.em	Δen	Δla	Ser
	145	1		1		150				0111	155	1110		A.J.1	nia	160
	Asp	Cys	Val	Val	Ile	Val	Thr	Thr	Pro	Asp		Ser	Ala	Ile	Thr	
30	_	-	•		165					170					175	-
	Ala	Tyr	Ala	Cys	Ile	Lys	Ile	Asn	Ser	Lys	Asn	Lys	Asp	Glu	Leu	Phe
				180					185					190		
	Leu	Ile		Asn	Met	Val	Ala		Pro	Lys	Glu	Gly	_	Ala	Thr	Tyr
35	<b>63</b>	<b>.</b>	195	<b>5</b> 1	<b>.</b>			200	_	_			205	_		
33	GIU	Arg 210	ren	Pne	ràs.	Val	A1a 215	Lys	Asn	Asn	Ile		Ser	Leu	GLu	Leu
	Uic		T.e.ii	Glv	λla	Ile		λαπ	Cor	e	T and	220	7	N	T	1751
	225	- 7 -	Deu	GLY	AIG	230	GIU	ASII.	SET	Ser	235	Tea	пуs	Arg	ıyı	240
		Glu	Arg	Lvs	Ile	Leu	Ara	Lvs	Ile	Ala		Asn	Asp	Leu	Phe	
40			-	•	245					250					255	
	Gln	Ser	Ile	Asp	Gln	Ile	Ala	Ser	Leu	Leu	Val	Ser	Lys	Leu	Glu	Thr
				260					265					270		
	Gly	Thr	Leu	Glu	Ile	Pro	Lys	Glu	Gly	Leu	Lys	Ser	Phe	Phe	Lys	Arg
4.5			275					280					285			
45	Leu		Lys	Tyr	Leu	Gly	•									
		290														

# (2) INFORMATION FOR SEQ ID NO:121:

- 50 (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 372 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- 55 (ii) MOLECULE TYPE: protein

```
(iii) HYPOTHETICAL: YES
```

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

#### (ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION 1...372

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:121:

				~					DDQ	10 1	<b>40.1</b> 2					
	Leu 1	Gli	ı Pro	Ser	: Arg	Asn	Arg	Leu	Lys	His	Ala	Ala	Phe	Phe		Gly
15	Leu	Phe	e Ile	Val	. Leu	Phe	Leu	Ile	Ile 25	Met	Lys	His	Gln	Thr 30	15 Ser	Pro
	Тут	Ala	Phe	Thr	His	Asn	Gln	Ala 40		Val	Thr	Gln	Thr 45	Pro	Pro	туг
20		50					55					60	Leu			His
	65					70					75					Tyr 80
25					85					90					95	Asn
25				100					105					110		Leu
			TTD					120					125			Leu
30		T20					135					140				
	145					150		Trp			155					160
35					165			His		170					175	
				TRO				Ser Met	185					190		
			195					200 Lys					205			
40		210					215	Leu				220				
	225					230		Val			235					240
45					245			Thr		250					255	
				<b>460</b>				Lys	265					270		
			2/5					280 Tyr					285			•
50		250					295	Trp				300				
•	305					310		Leu			315					320
55					325			His		330					335	
													-ul	- Y -		4 γ ⊥

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345 Asn Arg Ser His Ile Lys His Ile Arg Phe Asn Met Ala Tyr Leu Asn 360 Ser Leu Leu Lys 5 370 (2) INFORMATION FOR SEQ ID NO:122: (i) SEQUENCE CHARACTERISTICS: 10 (A) LENGTH: 978 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein 15 (iii) HYPOTHETICAL: YES (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori 20 (ix) FEATURE: (A) NAME/KEY: misc feature (B) LOCATION 1...978 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:122: Met Lys Lys Arg Lys His Val Ser Lys Lys Val Phe Asn Val Ile Ile Leu Phe Val Ala Val Phe Thr Leu Leu Val Val Ile His Lys Thr Leu 30 Ser Asn Gly Ile His Ile Gln Asn Leu Lys Ile Gly Lys Leu Gly Ile 40 Ser Glu Leu Tyr Leu Lys Leu Asn Asn Lys Leu Ser Leu Glu Val Glu 55 Arg Val Asp Leu Ser Ser Phe Phe His Gln Lys Pro Thr Lys Lys Arg Leu Glu Val Ser Asp Leu Ile Lys Asn Ile Arg Tyr Gly Ile Trp Ala Val Ser Tyr Phe Glu Lys Leu Lys Val Lys Glu Ile Ile Leu Asp Asp 40 105 Lys Asn Lys Ala Asn Ile Phe Phe Asp Gly Asn Lys Tyr Glu Leu Glu 120 Phe Pro Gly Ile Lys Gly Glu Phe Ser Leu Glu Asp Asp Lys Asn Ile 135 45 Lys Leu Lys Ile Ile Asn Leu Leu Phe Lys Asp Val Lys Val Gln Val 155 Asp Gly Asn Ala His Tyr Ser Pro Lys Ala Arg Lys Met Ala Phe Asn 165 170 Leu Ile Val Lys Pro Leu Val Glu Pro Ser Ala Ala Ile Tyr Leu Gln 50 185 190 Gly Leu Thr Asp Leu Lys Thr Ile Glu Leu Lys Ile Asn Thr Ser Pro 200 205 Met Lys Ser Leu Ala Phe Leu Lys Pro Leu Phe Gln Arg Gln Ser Gln 215 220 Lys Asn Leu Lys Thr Trp Ile Phe Asp Lys Ile Gln Phe Ala Ser Phe 55

	225	5				.230	)				235	,				240
	Lys	; Ile	e Asr	Asr.	Ala 245	Leu ;	ı Ile	Lys	Ala	Asr 250	ı Phe	Thi	Pro	Ser	Glu 255	Phe
5	Ile	e Pro	Ser	Let 260	Lev	ı Glu	Asr.	Ser	Val 265	. Val		Ala	Thr	Leu 270	Ile	Lys
	Pro	Ser	val 275	. Val	. Phe	Asn	Asp	Gly 280		Ser	Pro	Ile	Lys 285	Met	Asp	Lys
		290	)				295	;				300	Gln	Pro		Lys
10	305					310					315					Ser 320
					325					330	) ` .				335	Pro
15				340	'	Ser			345	;				350	Lys	
			355	•				360					365	•		Lys
20		370	)			Leu	375					380				
20	303					Gln 390					395					400
					405					410					415	
25				420		Asp			425					430		
			435			Ile		440					445			
30		450				His	455					460				
30	465					Asp 470					475					480
					485	Leu				490					495	
35				500		Phe			505					510		
٠			515			Phe		520					525			
40		230				Ser	535					540				
	343					Pro 550					555					560
					565	Lys				570					575	
45				580		Tyr	•		585					590		
			595			Val		600					605			
50		610				Tyr	615					620				
	625		FIIC	Gry	ser	Ile 630	ASI	гуs	Asp	GIu		Ser	Val	Tyr		
		Lys	Ser	Ile	Ser 645	Ile	Lys	Val	Lys	Gly 650	635 Asp	Gln	Lys		Ile 655	640 Thr
55	Leu	Asn	Asn	Ile 660	Asp	Leu	Ser	Ile	Asp 665		Phe	Leu	Asp	Ser 670	Lys	Met

	Pro	Ala	Ile 675	Ala	Gly	Leu	Phe	Ser 680	Lys	Glu	Arg	Lys	Glu 685	Lys	Pro	Ser
	Ser	Lys 690	Glu	Ile	Gln	Asp	Glu 695	Asp	Val	Phe	Ile	Ser		Lys	Gln	Arg
5	Tyr 705	Glu	Lys	Ala	His	Lys 710	Ile	Ile	Pro	Ile	Ser 715	Thr	Arg	Ile	His	Ala 720
					725	Ile				730					735	
10 -				740		Gln			745					750		_
			755			Met		760					765		_	
		770				Ser	775					780				
15	785					Gly 790			•		795					800
					805	Glu				810					815	
20				820		Asn			825					830		
•			835			Asn		840			•		845			
		850				Val	855					860	-			
25	865					Val 870					875			_		880
					885					890					895	Ser
30				900		Ser			905					910		
			915			Lys		920				•	925			
		930				Lys	935					940				_
35	945	•				Phe 950					955					960
	Asp	Ile	Ile	Val	Asp 965	Glu	Val	Lys	Lys	Asn 970	Ile	qeA	Ser	Lys	Arg 975	Lys
40	Leu	Lys						•					-			÷

(2) INFORMATION FOR SEQ ID NO:123:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 477 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

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## (ix) FEATURE:

- (A) NAME/KEY: misc_feature
  (B) LOCATION 1...477

#### 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:123:

									-							
	_									าก						e Thi
1	•			20					25					2.0	е Гу	s Glr
			33					40					A E			o Pro
1							22					60				s Glu
1:	. 65					, ,					76					s Ser 80
					00					90						r Thr
20	-			100					105					446	Met	: Lys
				,				120	1				100	a Asr	Ala	a Ser
			•				T 7 2					3 · A A	Туг	Lys		5 Tyr
25	145					<b>1</b> 30						Asn	Val		•	Gly 160
					103					170	Ser	Ala				Ser
30				100					185					700	Glr	Val
			~ ~ ~					200					205	Met	Ile	Ala
25							413					220	Lys	Arg		Thr
35	225					230					225					Leu 240
				Gly	233					250					^	Phe
40				Gln 260					765					~-~	Leu	
				Leu				280					205	Leu		
45				Gln			295					200				
43				Asn		310					71"					
										ママハ						Arg
50	Phe			740					145					250	Thr	
				Ile				460					~ ~ -	Lys		
55				Gly									Ala			
55	Leu	Glu	Gln	Glu :	Lys .	Asp	Glu	Gln	Leu	Tyr	Arg	Lys	Ser	Leu	Asp	Ile

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	385					390					395					400
				Lys	405					410					415	
5				Ala 420					425					430		
			435	Tyr				440					445			
		450		Leu			455					460		Ala	Asn	Tyr
10	11e 465	Phe	Asn	Ser	Gly	His 470	Lys	Ile	Asp	Asp	Tyr 475	Val	His			
	(2)	INF	ORMA	TION	FOR	SEQ	ID _. 1	NO:1	24:							
15		(i	()	QUENCA) LI B) T D) T	ENGT YPE :	H: 4: amiı	12 an	mino cid		ds						
20		(ii)	) MO	LECU	LE T	YPE:	pro	tein								
		(iii	) HY	POTH	ETIC	AL: Y	YES									
25		(vi)		IGINA A) O				icoba	acte:	r py:	lori					
		(ix		ATURI A) Ni		KEY:	mis	c fea	atur	9						
30			(1	B) L(	CAT:	ION :	14	412		-			٠		•	
	*			QUEN												
	1			Phe	5					10					15	
35				Ala 20					25					30		
			35	Gln				40					45			
10		50		Leu			55					60				
	65			Lys		70					75					80
15				Ser	85	٠.				90					95	
:5				Gly 100					105					110	•	
			115	Lys				120					125			
0		130		Thr			135					140				
	145			Tyr		150					155				•	160
5	116	пÀЗ	Asn	Leu	165	ASD	Inr	Leu	Tyr	GIn 170	Ala	Asn	His	ser	Ser 175	ser

				180					185					190	)		
	Glu	Ile	Gln 195	Lys	Asn	Asp	Leu	Glu 200		Ala	Leu	Ser	Ser 205		His	Tyr	
5	Ser	Met 210	Gly	Glu	Leu	Thr	Phe 215	Lys	Glu	Asn	Glu	Ile 220	Leu	Ser	Ile	Ala	
	Pro 225	Lys	Asn	Phe	Glu	Phe 230		Asn	Glu	Gln		Leu		Asn	Ile	Ser	
		Thr	Asn	Tyr	Asp		Ala	Ile	Ala		235 Leu	Asp	Glu	Glu	Lys	240 Ala	
10	Gln	Lys	Asp	Ile	245 Thr	Leu	Ala	Lys	Lys	250 Ser	Phe	Leu	Glu	Asp	255 Ile	Asn	
	Val	Thr	Gly	260 Val	Tyr	Tyr	Phe	Arg	265 Ser	Lys	Gln	Tyr	Tyr	270 Asn	Tyr	Asp	
			275					280					285			Gln	
15		290					295					300				Ser	
	305					310					315					320	
20					325					330					335	Leu	
20				340					345					350		Lys	
	Ile	Ile	Lys 355	Gln	Asn	Glu	Lys	Ile 360	Ala	Gln	Ile	Tyr	Ala 365	Leu	Asp	Leu	
25	Lys	Thr 370	Asn	Gly	Asp	Tyr	Asn 375	Ala	Tyr	Tyr	Asn	Ala 380	Leu	Asn	Asp	Lys	
	Ile 385	Thr	Ile	Gln	Ile	Thr 390		Leu	Glu	Thr		Ser	Ala	Leu	Asn	Ser	
		Tyr	Leu	Ser	Leu 405	Gln	Asn	Leu	Lys		395 Leu	Glu				400	
30										410			•				
	(2)					SEQ											
		(i)				IARAC I: 13				ls							
35						amin GY:											
	•	(ii)				PE:											
40								-6711		•.							·
10						L: Y										,	
		(V1)				URCE SM:		.coba	cter	pyl	ori						
45		(ix)		TURE			_										
	٠					EY: ON 1			ture						,		
	•	(vi)							FIG. 7	D 170							
50	Met					SCRI											
•	Met .				5					10					15		
	Ser .			20 .					25					30			
55	Ser	Gly :	Lys	Lys	Phe '	Tyr :	Lys	Leu :	His :	Lys .	Asn	His	Gly	Ser	Glu	Thr	

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35 40 Glu Thr Lys Asn Asp Lys Lys Leu Tyr Asp Phe Thr Lys Asn Ser Gly 55 Leu Glu Gly Val Asp Leu Glu Lys Ser Pro Asn Leu Lys Ser His Lys Lys Ser Asp Lys Lys Phe Tyr Lys Gln Leu Ala Lys Asn Asn Ile Ala Glu Gly Val Ser Met Pro Ile Val Asn Phe Asn Lys Ala Leu Ser Phe 105 Gly Pro Tyr Phe Glu Arg Thr Lys Ser Lys Lys Thr Gln Tyr Met Asp 120 Gly Gly Leu Met Met His Ile Arg Phe 15 (2) INFORMATION FOR SEQ ID NO:126: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 309 amino acids (B) TYPE: amino acid 20 (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: YES 25 (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: 30 (A) NAME/KEY: misc feature (B) LOCATION 1...309 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:126: 35 Leu Met Pro Gln Asn Gln Leu Val Ile Thr Ile Ile Asp Glu Ser Gly Ser Lys Gln Leu Lys Phe Ser Lys Asn Leu Lys Arg Asn Leu Ile Ile Ser Val Val Ile Leu Leu Leu Ile Val Gly Leu Gly Val Gly Phe Leu 40 40 Lys Phe Leu Ile Ala Lys Met Asp Thr Met Thr Ser Glu Arg Asn Ala 55 Val Leu Arg Asp Phe Arg Gly Leu Tyr Gln Lys Asn Tyr Ala Leu Ala 45 Lys Glu Ile Lys Asn Lys Arg Glu Glu Leu Phe Ile Val Gly Gln Lys Ile Arg Gly Leu Glu Ser Leu Ile Glu Ile Lys Lys Gly Ala Asn Gly 105 Gly His Leu Tyr Asp Glu Val Asp Leu Glu Asn Leu Ser Leu Asn 50 . 120 Gln Lys His Leu Ala Leu Met Leu Ile Pro Asn Gly Met Pro Leu Lys 135 140 Thr Tyr Ser Ala Ile Lys Pro Thr Lys Glu Arg Asn His Pro Ile Lys

Lys Ile Lys Gly Val Glu Ser Gly Ile Asp Phe Ile Ala Pro Leu Asn

165 170 Thr Pro Val Tyr Ala Ser Ala Asp Gly Ile Val Asp Phe Val Lys Thr 185 Arg Ser Asn Ala Gly Tyr Gly Asn Leu Val Arg Ile Glu His Ala Phe 200 Gly Phe Ser Ser Ile Tyr Thr His Leu Asp His Val Asn Val Gln Pro 215 Lys Ser Phe Ile Gln Lys Gly Gln Leu Ile Gly Tyr Ser Gly Lys Ser 230 Gly Asn Ser Gly Gly Glu Lys Leu His Tyr Glu Val Arg Phe Leu Gly 10 Lys Ile Leu Asp Ala Glu Lys Phe Leu Ala Trp Asp Leu Asp His Phe 265 Gln Ser Ala Leu Glu Glu Asn Lys Phe Ile Glu Trp Lys Asn Leu Phe 15 280 Trp Val Leu Glu Asp Ile Val Gln Leu Gln Glu His Val Asp Lys Asp 295 Thr Leu Lys Gly Gln 20 (2) INFORMATION FOR SEQ ID NO:127: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 332 amino acids 25 (B) TYPE: amino acid (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein 30 (iii) HYPOTHETICAL: YES (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc feature (B) LOCATION 1...332 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:127: 40 Val Leu Tyr Phe Leu Thr Ser Leu Phe Ile Cys Ser Leu Ile Val Leu Trp Ser Lys Lys Ser Met Leu Phe Val Asp Asn Ala Asn Lys Ile Gln Gly Phe His His Ala Arg Thr Pro Arg Ala Gly Gly Leu Gly Ile Phe 40 Leu Ser Phe Ala Leu Ala Cys Tyr Leu Glu Pro Phe Glu Met Pro Phe Lys Gly Pro Phe Val Phe Leu Gly Leu Ser Leu Val Phe Leu Ser Gly 50 Phe Leu Glu Asp Ile Asn Leu Ser Leu Ser Pro Lys Ile Arg Leu Ile 90 Leu Gln Ala Val Gly Val Val Cys Ile Ile Ser Ser Thr Pro Leu Val 105 Val Ser Asp Phe Ser Pro Leu Phe Ser Leu Pro Tyr Phe Ile Ala Phe

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			115					120					125			
	Leu	Phe	Ala	Ile	Phe	Met	Leu	Val	Gly	Ile	Ser	Asn	Ala	Ile	Asn	Ile
		130					135					140				
_	Ile	Asp	Gly	Phe	Asn	Gly	Leu	Ala	Ser	Gly	Ile	Cys	Ala	Ile	Ala	
•5	145		_			150					155					160
	Leu	Val	Ile	His		Ile	Asp	Pro	Ser		Leu	Ser	Cys	Leu		Ala
	_			_	165	_,		•	_	170		_	_		175	
	Tyr	Met	val		GIĀ	Phe	Met	vaı		Asn	Pne	Pro	ser	_	rys	IIe
10	nh-	7	<i>α</i> 1	180	C1	C1.,	21-	TT	185	T	<b>03</b>	T	17-1	190	<b>~</b> 3	T1.
10	PILE	Tien	195	Map	GLY	Gly	Ата	200	FIIE	Leu	GIY	Leu	205	Cys	GIY	116
	Car	T.e.11		Hig	T.e.11	Ser	T.em		Gln	Lire	T16	Ser		Dhe	Dhe	Glv
	Jer	210	2004	*****			215	014	<b>Q_111</b>	Lys	110	220	Val	FIIC		O _T y
	Leu		Leu	Met	Leu	Tyr		Val	Ile	Glu	Val		Phe	Ser	Ile	Leu
15	225					230					235					240
	Arg	Arg	Lys	Ile	Lys	Arg	Gln	Lys	Ala	Thr	Met	Pro	Asp	Asn	Leu	His
	•	_	_		245					250					255	
	Leu	His	Thr	Leu	Leu	Phe	Lys	Phe	Leu	Gln	Gln	Arg	Ser	Phe	Asn	Tyr
				260					265					270		
20	Pro	Asn	Pro	Leu	Cys	Ala	Phe	Ile	Leu	Ile	Leu	Cys	Asn	Leu	Pro	Phe
			275					280					285			
	Ile		Ile	Ser	Val	Leu		Arg	Leu	Asp	Ala		Ala	Leu	Ile	Val
		290	_	٠ -			295	_		_		300	_		_	_
25		Ser	Leu	vaı	Pne	Ile	Ala	Cys	Tyr	Leu		GIY	Tyr	Ala	ıyr	
25	305	N	~1 m	1707	Crea	310 Ala	T 011	G1.,	T		315	Dho				320
	ASII	Arg	GIII	vai	325	ALA	ren	GIU	гÃЗ	330	Ala	Pne				
					323											
	(2)	INFO	ORMA'	rion	FOR	SEQ	ID 1	NO:12	28:							
30	,					~										
*		(i)	SE	QUEN	CE CI	HARA	CTER.	ISTIC	CS:							
			(2	A) LI	engti	H: 2'	71 ar	nino	acio	ds						
			(1	B) T	PE:	amiı	no a	cid								
25			(1	D) T	OPOL	OGY:	line	ear								
35																
•		(ii)	MO	PECOI	LE T	YPE:	prot	tein								
		, , , , ,			enta:	AT . 1	ZPÓ								•	
		(111)	HI	POIM	51 1 C	AL: 1	LES									
40		(sri )	OB.	CTN	AT. SC	OURC	₹•			•						
		( • • •				ISM:		i coba	acte	r pv	lori					
			•							- F2.						
		(ix)	FE2	ATURI	Z :											
			(2	A) NZ	AME/I	KEY:	mis	c_fea	atur	2						
45			(1	B) L(	CAT:	ION :	ι:	271		•						
		(xi)	SE	QUEN	CE DI	ESCR:	IPTIC	ON: S	SEQ .:	ID N	0:128	3:				
					_							· _			_	
50		Asn	Ile	Phe	Lys	Arg	Ile	Ile	Cys		Thr	Ala	Ile			Gly
50	1	D1	<b>3</b>	7	5	3	22-	T	T7.0 -	10	•		<b>T</b>		. 15	n
	rne	rne	ASD	Leu 20	ьeu	Asp	ATA	тАв		HIS	гÀг	GIU	ràs		GIU	Asp
	uie	Lare	710		Δτα	Glu	T.e.	Lve	25 Val	G1v	Δl =	λαν	Dro	30 Val	Pro	Hie
	1112	Lys	35		AL 9	GIU	<b>⊥</b> cu	195 40	va_	GIY	TTA	usii	45	V	-10	****
55	Ala	Gln		Leu	Gln	Ser	Val		asA	Asp	Leu	Lvs		Lys	Glv	Ile
									_	-				-	-	

Lys Leu Val Ile Val Ser Phe Thr Asp Tyr Val Leu Pro Asn Leu Ala Leu Asn Asp Gly Ser Leu Asp Ala Asn Tyr Phe Gln His Arg Pro Tyr 90 Leu Asp Arg Phe Asn Leu Asp Arg Lys Met His Leu Val Gly Leu Ala 105 Asn Ile His Val Glu Pro Leu Arg Phe Tyr Ser Gln Lys Ile Thr Asp 120 Ile Lys Asn Leu Lys Lys Gly Ser Val Ile Ala Val Pro Asn Asp Pro 135 Ala Asn Gln Gly Arg Ala Leu Ile Leu Leu His Lys Gln Gly Leu Ile 150 155 Ala Leu Lys Asp Pro Ser Asn Leu Tyr Ala Thr Glu Phe Asp Ile Val 15 170 Lys Asn Pro Tyr Asn Ile Lys Ile Lys Pro Leu Glu Ala Ala Leu Leu 185 Pro Lys Val Leu Gly Asp Val Asp Gly Ala Ile Ile Thr Gly Asn Tyr 200 Ala Leu Gln Ala Lys Leu Thr Gly Ala Leu Phe Ser Glu Asp Lys Asp 215 Ser Pro Tyr Ala Asn Leu Val Ala Ser Arg Glu Asp Asn Ala Gln Asp 230 235 Glu Ala Ile Lys Ala Leu Ile Glu Ala Leu Gln Ser Glu Lys Thr Arg 25 245 250 Lys Phe Ile Leu Asp Thr Tyr Lys Gly Ala Ile Ile Pro Ala Phe 265 (2) INFORMATION FOR SEQ ID NO:129: 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 316 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear 35 (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: YES 40 (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc_feature 45 (B) LOCATION 1...316 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:129: Met Gln Glu Phe Ser Leu Trp Cys Asp Phe Ile Glu Arg Asp Phe Leu 50

Glu Asn Asp Phe Leu Lys Leu Ile Asn Lys Gly Ala Ile Cys Gly Ala 20 25 30 Thr Ser Asn Pro Ser Leu Phe Cys Glu Ala Ile Thr Lys Ser Ala Phe

Tyr Gln Asp Glu Ile Ala Lys Leu Lys Gly Lys Lys Ala Lys Glu Ile

		50	Thr	Lou	ה ו ת	T.ou	55	Nam	T10	Ton	C1 n	60 21-2	co~	Ca*	71-	Lan
	65					70	-	_			Gln 75		•			80
<b>5</b>	Met	Pro	Leu	Tyr	Glu 85	Lys	Asp	Pro	Asn	Asn 90	Gly	Tyr	Ile	Ser	Leu 95	Glu
	Ile	Asp	Pro	Phe 100	Leu	Glu	Asp	Asp	Ala 105	Ile	Lys	Ser	Ile	Asp 110	Glu	Ala
	Lys	Arg	Leu 115	Phe	Lys	Thr	Leu	Asn 120	Arg	Pro	Asn	Val	Met 125	Ile	Lys	Val
10	Pro	Ala 130		Glu	Ser	Ala	Phe 135		Val	Ile	Ser	Ala 140		Ala	Gln	Ala
	Ser 145		Pro	Ile	Asn	Val		Leu	Val	Phe	Ser 155		Lys	Ile	Ala	Gly 160
15		Ile	Ala	Gln	Ile 165		Ala	Lys	Glu	Ala 170	Arg	Lys	Arg	Ala	Val 175	Ile
	Ser	Val	Phe	Val		Arg	Phe	Asp	Lys 185		Ile	Asp	Pro	Leu 190		
	Gln	Asn	Leu 195		Ala	Gln	Ser	Gly 200		Met	Asn	Ala	Thr 205		Cys	Tyr
20	Tyr	Gln 210		Asn	Gln	His	Ala 215		Lys	Leu	Ile	Ser 220		Leu	Phe	Ala
	Ser 225		Gly	Val	Lys	Ser 230		Ser	Leu	Ala	Lys 235		Tyr	Tyr	Ile	Lys 240
25		Leu	Cys	Phe	Lys 245		Ser	Ile	Asn	Thr 250	Ala	Pro	Leu	Asp	Ala 255	
	Asn	Ala	Tyr	Leu 260		Asp	Pro	Asn	Thr 265		Сув	Gln	Thr	Pro 270		Lys
	Ile	Thr	Glu 275		Glu	Ala	Phe	Lys 280		Glu	Leu	Lys	Thr 285		Asn	Ile
30	Asp	Leu 290		Asn	Thr	Ala	Gln 295		Leu	Leu	Lys	Glu 300		Leu	Ile	Ala
	Phe 305		Gln	Ser	Phe	Glu 310	Lys	Leu	Leu	Ser	Ser 315					
35	(2)	INFO	ORMA!	rion	FOR	SEQ	ID I	NO:1	30:							
		(i)		_		HARAG				is						
<b>4</b> 0			(1	3) T	YPE:	amiı	no a	cid		-					-	

- (ii) MOLECULE TYPE: protein
- (iii) HYPOTHETICAL: YES
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:

- (A) NAME/KEY: misc_feature
  - (B) LOCATION 1...260
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:130:
- 55 Met Lys Thr Asn Gly His Phe Lys Asp Phe Ala Trp Lys Lys Cys Phe

	1				5					10					15	
				20					25					30		Ile
:5			35					40			Asn		45	Pro		
	Glu	Lys 50	Val	Gln	Ala	Leu	Asp 55	Glu	Lys	Ile	Leu	Leu 60	Leu	Arg	Pro	Ala
	Phe 65	Gln	Tyr	Ser	Asp	Asn 70	Ile	Ala	Lys	Glu	Tyr 75	Glu	Asn	Lys	Phe	Lys 80
10	Asn	Gln	Thr	Thr	Leu 85	Lys	Val	Glu	Glu	Ile 90	Leu	Gln	Asn	Gln	Gly 95	Tyr
	Lys	Val	Ile	Asn 100	Val	Asp	Ser	Ser	Asp	Lys	Asp	Asp	Phe	Ser	Phe	Ala
15	Gln	Lys	Lys 115	Glu	Gly	Tyr	Leu	Ala 120	Val	Ala	Met	Asn	Gly 125	Glù	Ile	Val
٠	Leu	Arg 130	Pro	Asp	Pro	Lys	Arg	Thr	Ile	Gln	Lys	Lys 140	Ser	Glu	Pro	Gly
	145					150					Glu 155	Arg				160
20					165					170	Pro				175	Ser
	Leu	Asp	Ser	Phe 180	Thr	Met	Asp	Leu	Ser 185	Glu	Leu	Asp	Ile	Gln 190	Glu	Lys
25	Phe	Leu	Lys 195	Thr	Thr	His	Ser	Ser 200	His	Ser	Gly	Gly	Leu 205	Val	Ser	Thr
		210					215				Ala	220	Lys			
	225					230					Mèt 235					240
30					Glu 245	Ser	Tyr	Gln	Lys	Asp 250	Ala	Lys	Glu	Leu	Lys 255	Asn
	Lys	Arg	Asn	Arg 260												
35	(2)	INFO	RMAT	CION	FOR	SEQ	ID N	IO:13	1:							
		(i)						STIC								
40			(E	i) TY i) TO	PE:	amin	o ac		aci	.ds			·			
		(ii)		ECUL												

- (iii) HYPOTHETICAL: YES 45

(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori

(ix) FEATURE:

- (A) NAME/KEY: misc_feature (B) LOCATION 1...1382
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:131:
- 55 Leu Asn Phe Asn Asn Leu Thr Ala Asn Gly Ala Leu Asn Phe Asn Gly

	1				5					10					15	•
	-	Ala	Pro	Ser 20		Thr	Lys	Ala			Asn	Val	Ser	Gly 30		Phe
5			35			Gly		40					45			
		50				Ser	55					60				
	65					Ser 70					75					80
10					85	Gln				90					95	
				100		Ile			105					110	•	
15			115			Gly Thr		120					125			
		130				Gln	135			٠.		140			_	
20	145			, .		150 Thr					155					160
					165	Ser				170					175	
_ :				180		Leu	-		185					190		
25	Ser		195 Glu	Asn	Leu	Lys		200 Leu	Leu	Gly	Ile	Leu	205 Ser	Gln	Asn	Ser
		210 Thr	Leu	Lys	Glu	Met	215 Ile	Glu	Ser	Asn		220 Leu	Asp	Asn	Ile	
30	225 Asn	Ile	Asn		Val 245	230 Leu	Gln	Leu	Leu		235 Lys	Ile	Lys	Ile		240 Gln
	Ala	Gln	Lys			Leu	Leu	Glu	Thr 265	250 Ile	Asn	His	Leu	Thr 270	255 Asp	Asn
35	Ile	Asn	Gln 275		Phe	Asn	Asn	Gly 280	_	Leu	Val	Ile	Gly 285		Thr	Gln
		290				Ser	295				-	300		_		-
40	305	-				Ala 310					315					320
40					325	.Gln				330	•			_	335	•
				340		Phe			345			_		350		
45			355			Ala Asn		360					365			
. •		370				Ile	375					38.0				
50	385					390 Gly					395					400
					405	Gln				410					415	
				420		Ser			425					430		
55			435				-	440					445		•	

•	Thi	Le: 450	ı Gl	y Glı	n Lei	ı Ile	Gl ₃	/ Glr	Ası	ı Ası	ı Leı	1 As ₁		o Lei	ı Le	u Asn
	Asr 465	ı Sei	c Gly	y Val	l Met	Asr 470	Glu	ı Ile	e Glr	a Ası	ı Ile	: Ile	Se:	r Glı	ı Ly	s Leu
5	Ser	Ile	Phe	e Gly	Ası 485	ı Phe		Thr	Pro	Ser 490	475 Ile	lle	e Glu	ı Ası		480 Leu
	Ala	Lys	Gli	1 Sei 500	. Lev		Ser	Met	Lev 505	a Asp	Asp	Lys	Gl _y			ı Asn
10	Phe	: Ile	Gl ₃	/ Gly		: Ile	Asp	Ala 520	Ser		l Leu	Ser			) Let	ı Gly
	Val	. Ile 530	Let		a Asp	Ile	Thr. 535	Asn	Pro	Pro	Thr			ı Glr	Lys	qaA a
	Ile 545	Gly	v Val	. Val	Ala	Asn 550	Asp		Leu	Asn			Leu	ı Gly	glr Glr	a Asp
15			Lys	Lys	Leu 565	Glu		Gln	Gly			Ser	Asn	ı Ile	Ile	560. Asn
	Asn	Val	Ile	Ser 580	Gln		Gly	Leu	Ser	570 Gly	val	Tyr	Asn			Leu
20	Gly	Ser	Val	Leu		Pro	Ser	Leu	585 Gln	Asn	Ala	Leu			Asn	Asp
	Leu	Gly 610	Thr		Leu	Ser	Pro 615	600 Arg	Gly	Leu	His			Trp	Gln	Lys
•	Gly 625	Tyr	Phe	Asn	Phe	Leu 630	Ser		Gly	Tyr	Val	620 Phe	Val	Asn	Asn	Ser
25			Ser	Asn	Ala 645	Thr		Gly	Ser	Leu	635 Asn	Phe	Val	Ala		640 Lys
	Ser	Ile	Ile	Phe	Asn		Asp	Asn	Thr 665	650 Ile	Asp	Phe	Ser		655 Tyr	Gln
30	Gly	Ala	Leu 675	Ile		Ala	Ser	Asn 680	Gly	Val	Ser	Asn		670 Asn	Ile	Thr
	Thr	Leu 690	Asn	Ala	Thr	Asn	Gly 695	Leu	Ser	Leu	Asn		685 Gly	Leu	Asn	Asn
	Val 705	Ser	Val	Gln	Lys	Gly 710	Glu	Ile	Cys	Ile	Asn 715	700 Leu	Ala	Asn		Pro
35	Thr	Thr	Lys	Asn	Ser 725	Ser	Pro	Ala	Asn	Ser	Ser	Val	Thr	Pro	Thr	720 Asn
	Glu	Ser	Leu	Ser 740	Val	His	Ala	Asn	Asn 745	Phe	Thr	Phe	Leu		735 Thr	Ile
40	Ile	Ser	Asn 755	Gly	Ala	Ile	Asp	Leu 760	Ser	Gln	Val	Thr		750 Asn	Ser	Val
	Ile	Gly 770	Thr	Leu	Asn	Leu	Asn 775	Glu	Asn	Ala	Thr	Leu 780	765 Gln	Ala	Asn	Asn
. ,	Leu 785	Thr	Ile	Thr	Asn.	Ala 790		Asn	Asn	Ala	Ser 795	Asn	Ser	Thr	Ala	
45	Ile	Asp	Gly	Asn	Phe 805	Thr	Leu	Asn	Gln	Gln 810	Ala	Thr	Leu	Ser		800 Asn
	Ala	Ser	Gly	Leu 820	Asn	Val	Met	Gly	Asn 825	Phe	Asn	Ser	Tyr	Gly 830	815 Asp	Leu
50	Val	Phe	Asn 835	Leu	Ser	His	Ser	Val 840	Ser	His	Ala	Ile	Ile 845	Asn	Thr	Gln
		030				Met	855	Asn				860	Ile			
	003					Val 870	Gly				Leu 875	Ile				000
55	Ala	Ile	Tyr	Tyr	Gly	Tyr	Asn	Asn	Gln	Ile	Thr	Gly	Gly	Ser	Ser	880 Leu

					885					890			- 1		895	•
٠.				900					905					910	_	His
5			915					920					925			Ser
	Val	Lys 930	Asp	Gly	Gly	Leu	Val 935	Val	Gly	Phe	Lys	Asp 940	Ser	Gln	Asn	Gln
	945		Tyr	•		950				_	955	=				960
10	•				965			*		970					975	Ile
				980					985	_				990		Gly
15			995					1000	0				100	5		Gly
		101	0				101	5				102	0			Asp
20	1025	5				103	)				103	5				Ala 1040
20			Asn		104	5				105	0				105	5
			Gln	1060	)				1069	5				1070	)	
25			Arg 107!	5				108	D .				108	5		_
	-	109	0	_			109	5			_	110	ס		-	Tyr
	1109	5				1116	)				1119	5				Gly 1120
30					112	5	_	_		113	0		_	_	1135	
			Tyr	1140	)				1145	5			_	1150	)	
35			115	5				1160	0				1169	5	_	Ser
		1170	0				117	5				1180	)			Ser
	1185	5				1190	כ				1199	5				Phe 1200
<b>4</b> 0				•	120	5				1210	ס				1215	
			Thr	1220	)				1225	5		_	_	1230	)	
45			Lys 1235	5 .			-	1240	)				1245	5		
		1250				,	125	5				1260	)			
	1265	5				1270	)				1275	5				Val 1280
50			Ile		1285	5				1290	)				1295	5 `
			Tyr	1300	)				1305	5				1310	)	
55	Ser	Met		Asp				Arg 1320		Ile	Gly		Asn 1325		Leu	Ser

Tyr Arg Asp Gly Gly Arg Tyr Asn Thr Phe Ala Ser Ile Ile Thr Gly
1330 1335 1340

Gly Glu Ile Arg Leu Phe Lys Thr Phe Tyr Val Asn Ala Gly Ile Gly
1345 1350 1355 1360

Ala Arg Phe Gly Leu Asp Tyr Lys Asp Ile Asn Ile Thr Gly Asn Ile
1365 1370 1375

Gly Met Arg Tyr Ala Phe
1380

- 10 (2) INFORMATION FOR SEQ ID NO:132:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 262 amino acids
    - (B) TYPE: amino acid
- 15 (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

- 20
  - (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:
- 25 (A) NAME/KEY: misc_feature
  - (B) LOCATION 1...262
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:132:
- 30 Met Lys Lys Ile Gly Leu Ser Leu Cys Leu Val Leu Ser Leu Gly Phe
  1 5 10 15
  Leu Lys Ala His Glu Val Ser Ala Glu Glu Ile Ala Asp Ile Phe Tyr
  20 25 30
- Lys Leu Asn Ala Lys Glu Pro Lys Met Lys Ile Asn His Thr Lys Gly
  - Phe Cys Ala Lys Gly Val Phe Leu Pro Asn Pro Gln Ala Arg Glu Asp 50 55 60
  - Leu Glu Val Pro Leu Leu Asn Glu Lys Glu Ile Pro Ala Ser Val Arg
    65 70 75 80
- 40 Tyr Ser Leu Gly Gly Val Ala Met Asp Asp Lys Ser Lys Val Arg Gly
  85 90 95
  - Met Ala Leu Lys Leu Glu Asn Gln Asn Ala Ser Trp Thr Met Val Met
    100 105 110
- Leu Asn Thr Glu Ile Asn Phe Ala Lys Asn Pro Glu Glu Phe Ala Gln
  45 115 120 125
  - Phe Phe Glu Met Arg Leu Pro Lys Asn Gly Lys Val Asp Glu Ala Arg
    130 135 140
- Ile Lys Lys Leu Tyr Glu Glu Val Pro Ser Tyr Arg Asn Phe Ala Ala
  145 150 155 160
- 50 Tyr Met Lys Thr Ile Gly Ile Ser Ser Ser Val Ala Asn Thr Pro Tyr
  165 170 175
  - Tyr Ser Val His Ala Phe Lys Phe Lys Asp Lys Lys Glu Lys Leu Leu 180 185 190
- Pro Ala Arg Trp Lys Phe Val Pro Lys Glu Gly Val Lys Tyr Leu Asn 195 200 205

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Pro Gln Glu Leu Lys Gln Lys Asp Ser Asn Tyr Leu Leu Ser Ser Phe 215 Gln Gln His Leu Lys Asn Lys Pro Ile Glu Tyr Gln Met Tyr Leu Val 230 235 Phe Ala Asn Gln Asn Asp Ala Thr Asn Asp Thr Thr Ala Leu Trp Lys 250 Gly Ser Ile Arg Asn Tyr 260

- 10 (2) INFORMATION FOR SEQ ID NO:133:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 246 amino acids
    - (B) TYPE: amino acid
- 15 (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES

20

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
- (ix) FEATURE:

195

- 25 -(A) NAME/KEY: misc feature
  - (B) LOCATION 1...246
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:
- 30 Met Lys Gln Phe Lys Lys Lys Pro Lys Lys Ile Lys Arg Ser His Gln Asn Gln Lys Thr Ile Leu Lys Arg Pro Leu Trp Leu Met Pro Leu Leu Ile Gly Gly Phe Ala Ser Gly Val Tyr Ala Asp Gly Thr Asp Ile Leu 35 Gly Leu Ser Trp Gly Glu Lys Ser Gln Lys Val Cys Val His Arg Pro Trp Tyr Ala Ile Trp Ser Cys Asp Lys Trp Glu Glu Lys Thr Gln Gln 75 40 Phe Thr Gly Asn Gln Leu Ile Thr Lys Thr Trp Ala Gly Gly Asn Ala 85 90 Ala Asn Tyr Tyr His Ser Gln Asn Asn Gln Asp Ile Thr Ala Asn Leu 105 Lys Asn Asp Asn Gly Thr Tyr Phe Leu Ser Gly Leu Tyr Asn Tyr Thr 45 120 . Gly Gly Glu Tyr Asn Gly Gly Asn Leu Asp Ile Glu Leu Gly Ser Asn 135

Ala Thr Phe Asn Leu Gly Ala Ser Ser Gly Asn Ser Phe Thr Ser Trp 150 155 50 Tyr Pro Asn Gly His Thr Asp Val Thr Phe Ser Ala Gly Thr Ile Asn 170 Val Asn Asn Ser Val Glu Val Gly Asn Arg Val Gly Ser Gly Ala Gly

185 Thr His Thr Gly Thr Ala Thr Leu Asn Leu Asn Ala Asn Lys Val Thr 55 200

Ile Asn Ser Asn Ile Ser Ala Tyr Lys Thr Ser Gln Val Asn Val Gly 215 Asn Ala Asn Ser Val Ile Thr Ile Asn Ser Val Ser Leu Asn Gly Glu 235 Tyr Leu Gln Phe Phe Ser (2) INFORMATION FOR SEQ ID NO:134:

10 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 245 amino acids
- (B) TYPE: amino acid (D) TOPOLOGY: linear
- 15
- (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES
- (vi) ORIGINAL SOURCE: 20 (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:

25

55

- (A) NAME/KEY: misc feature
- (B) LOCATION 1...245

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:134: Met Ile Lys Lys Thr Leu Ala Ser Val Leu Leu Gly Leu Ser Leu Met Ser Val Leu Asn Ala Lys Glu Cys Val Ser Pro Ile Thr Arg Ser Val 20 Lys Tyr His Gln Gln Ser Ala Glu Ile Arg Ala Leu Gln Leu Gln Ser 40 Tyr Lys Met Ala Lys Met Ala Leu Asp Asn Asn Leu Lys Leu Val Lys 35 Asp Lys Lys Pro Ala Val Ile Leu Asp Leu Asp Glu Thr Val Leu Asn 70 Thr Phe Asp Tyr Ala Gly Tyr Leu Val Lys Asn Cys Ile Lys Tyr Thr 40 Pro Glu Thr Trp Asp Lys Phe Glu Lys Glu Gly Ser Leu Thr Leu Ile 100 105 Pro Gly Ala Leu Asp Phe Leu Glu Tyr Ala Asn Ser Lys Gly Val Lys 120 Ile Phe Tyr Ile Ser Asn Arg Thr Gln Lys Asn Lys Ala Phe Thr Leu 45 135 Lys Thr Leu Lys Ser Phe Lys Leu Pro Gln Val Ser Glu Glu Ser Val 150 155 Leu Leu Lys Glu Lys Gly Lys Pro Lys Ala Val Arg Arg Glu Leu Val 165 170 Ala Lys Asp Tyr Ala Ile Val Leu Gln Val Gly Asp Thr Leu His Asp 180 185 Phe Asp Ala Ile Phe Ala Lys Asp Ala Lys Asn Ser Gln Glu Gln Gln

200 Ala Lys Val Leu Gln Asn Ala Gln Lys Phe Gly Thr Glu Trp Ile Ile

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Leu Pro Asn Ser Leu Tyr Gly Thr Trp Glu Asp Gly Pro Ile Lys Ala 225 235 240

Trp Gln Asn Lys Lys 245

5

- (2) INFORMATION FOR SEQ ID NO:135:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 288 amino acids
- 10 (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
- 15 (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Helicobacter pylori
- 20 (ix) FEATURE:
  - (A) NAME/KEY: misc_feature
  - (B) LOCATION 1...288
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:135:

25

Leu Trp Cys Leu Lys Thr Pro Ile Ile Gly His Gly Met Lys Lys Lys 1 5 10 15

Ala Lys Val Phe Trp Cys Cys Phe Lys Met Ile Arg Trp Leu Tyr Leu
20 25 30

30 Ala Val Phe Phe Leu Leu Ser Val Ser Asp Ala Lys Glu Ile Ala Met 35 40 45

Gln Arg Phe Asp Lys Gln Asn His Lys Ile Phe Glu Ile Leu Ala Asp 50 55 60

Lys Val Ser Ala Lys Asp Asn Val Ile Thr Ala Ser Gly Asn Ala Ile 35 65 70 75 80

Leu Leu Asn Tyr Asp Val Tyr Ile Leu Ala Asp Lys Val Arg Tyr Asp 85 90 95

Thr Lys Thr Lys Glu Ala Leu Leu Glu Gly Asn Ile Lys Val Tyr Arg
100 105 110

40 Gly Glu Gly Leu Leu Val Lys Thr Asp Tyr Val Lys Leu Ser Leu Asn 115 120 125

Glu Lys Tyr Glu Ile Ile Phe Pro Phe Tyr Val Gln Asp Ser Val Ser 130 135 140

Gly Ile Trp Val Ser Ala Asp Ile Ala Ser Gly Lys Asp Gln Lys Tyr
45 145 150 155 160

145 150 155 160
Lys Ile Lys Asn Met Ser Ala Ser Gly Cys Ser Ile Asp Asn Pro Ile

165 170 175
Trp His Val Asn Ala Thr Ser Gly Ser Phe Asn Met Gln Lys Ser His

50 Leu Ser Met Trp Asn Pro Lys Ile Tyr Val Gly Asp Ile Pro Val Leu
195 200 205

Tyr Leu Pro Tyr Ile Phe Met Ser Thr Ser Asn Lys Arg Thr Thr Gly 210 215 220

Phe Leu Tyr Pro Glu Phe Gly Thr Ser Asn Leu Asp Gly Phe Ile Tyr 55 225 230 235 240

Leu Gln Pro Phe Tyr Leu Ala Pro Lys Asn Ser Trp Asp Met Thr Phe

245 250 255

Thr Pro Gln Ile Arg Tyr Lys Arg Gly Phe Gly Leu Asn Phe Glu Ala

260 265 270

Arg Tyr Ile Asn Ser Lys Thr Gln Val Phe Ile Gln Cys Ala Leu Phe

275 280 285

- (2) INFORMATION FOR SEQ ID NO:136:
- 10 (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 128 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- 15 (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:
    - (A) NAME/KEY: misc_feature
    - (B) LOCATION 1...128
- 25
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:136:
- Leu Met Phe Lys Lys Met Cys Leu Ser Leu Leu Met Ile Ser Gly Val
- Cys Val Gly Ala Lys Asp Leu Asp Phe Lys Leu Asp Tyr Arg Ala Thr
  - Gly Gly Lys Phe Met Gly Lys Met Thr Asp Ser Ser Leu Leu Ser Ile 35 40 45
- Thr Ser Met Asn Asp Glu Pro Val Val Ile Lys Asn Leu Ile Val Asn 35 50 55 60
  - Arg Gly Asn Ser Cys Glu Ala Thr Lys Lys Val Glu Pro Lys Phe Gly 65 70 75 80
  - Asp Lys Phe Lys Lys Glu Lys Leu Phe Asp His Glu Leu Lys Tyr Ser 85 90 95
- 40 Gln Gln Ile Phe Tyr Arg Leu Asp Cys Lys Pro Asn Gln Leu Leu Glu
  100 105 110
  - Val Lys Ile Ile Thr Asp Lys Gly Glu Tyr Tyr His Lys Phe Ser Lys
    115
    120
    125
- 45 (2) INFORMATION FOR SEQ ID NO:137:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 169 amino acids
    - (B) TYPE: amino acid
- 50 (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
- (ix) FEATURE:
- (A) NAME/KEY: misc_feature
  - (B) LOCATION 1...169
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:137:
- 10 Met Gln Ala Leu Lys Ser Leu Leu Glu Val Ile Thr Lys Leu Gln Asn 1 5 10 15

Leu Gly Gly Tyr Leu Met His Ile Ala Ile Phe Ile Ile Trp
20 25 30

Ile Gly Gly Leu Lys Phe Val Pro Tyr Glu Ala Glu Gly Ile Ala Pro
15 40 45

Phe Val Ala Asn Ser Pro Phe Phe Ser Phe Met Tyr Lys Phe Glu Lys 50 55 60

Pro Ala Tyr Lys Gln His Lys Met Ser Glu Ser Gln Ser Met Gln Glu 65 70 75 80

20 Glu Met Gln Asp Asn Pro Lys Ile Val Glu Asn Lys Glu Trp His Lys 85 90 95

Glu Asn Arg Thr Tyr Leu Val Ala Glu Gly Leu Gly Ile Thr Ile Met 100 105 110

Ile Leu Gly Ile Leu Val Leu Leu Gly Leu Trp Met Pro Leu Met Gly
25 115 120 125

Val Val Gly Gly Leu Leu Val Ala Gly Met Thr Ile Thr Thr Leu Phe 130 135 140

Phe Phe Ile His Asn Ala Arg Ser Val Cys Gln Ser Ala Phe Pro Met 145 150 155 160

30 Ala Phe Trp Gly Trp Lys Ala Ser Gly 165

- (2) INFORMATION FOR SEQ ID NO:138:
- 35 (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 487 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- 40 (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
- 45 (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:

50

- (A) NAME/KEY: misc feature
- (B) LOCATION 1...487
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:138:

Met Ile Glu Trp Met Gln Asn His Arg Lys Tyr Leu Val Val Thr Ile

5 10 15

55 Trp Ile Ser Thr Ile Ala Phe Ile Ala Ala Gly Met Ile Gly Trp Gly

	•			20					25							
	Gln	Tvr	Ser		Ser	Leu	Ast	Ser	25 Agn	Sar	. Ala	<b>λ</b> Ι	1,,,,	30 	Ø1	Gln
			35					40					45			
5		50					55					60				Lys
	Asp 65	Ala	Tyr	Ala	Glu	Ser	Ile	Pro	Asp	Phe	Lys 75	Glu	Leu	Thr	Glu	Asp 80
	Gln	Ile	Lys	Ala	Met 85	His	Leu	Glu	Lys	Ser	Ala	Leu	Asp	Ser		Ile
10	Asn	Gln	Ala	Leu 100	Leu	Arg	Asn	Phe	Ala	Leu	Asp	Leu	Gly	Leu	95 Gly	Ala
	Thr	Lys	Gln	Glu		Ala	Lys	Glu	105 Ile		Lys	Thr	Asn	110 Val	Phe	Gln
	7	<b>3</b>	115		<b>5</b> 1	_		120					125			
15		130					135					140				Gln
	Ser 145	His	Tyr	Arg	Pro	Lys	His	Phe	Glu	Glu			.Glu	Arg	Leu	Leu
	_		Gla	Taro	T10	150		· ·	1	_	155					160
					165			Leu		170					175	
20				180				Trp	185					190	Leu	
			195					200					205			Glu
25		210					215					220				Pro
	Thr 225	Ser	Phe	Lys	Thr	Arg 230	Ser	Leu	Tyr	Phe		Ala	Ser	Leu	Glu	Lys
		Asp	Leu	Lys	Glu		Glu	Glu	Tyr	Tyr	235 His	Lys	Asn	Lys	Val	240 Ser
30					245					250					255	
		*		260				Leu	265					270		
			275					Met 280					285			
35		290					295	Lys				300				
	Gln 305	Asp	Phe	Glu	Lys	Asn 310	Asn	Ser	Pro	Tyr		Ala	Glu	Ile	Thr	
		Leu	Thr	Ala	Leu		Pro	Leu	Glu	Val	315 Leu	Lys	Pro	Glu	Pro	320 Phe
40	Lys	Asp	Gly	Phe	325 Ile	Val	Val	Gln	Len	330 Val	Ser	Gl n	Tla	Lve	335	C1
				340					345					350		
			355					Lys 360					365			
45	Gln	Glu 370	Lys	Thr	Leu	Met	Ala 375	Leu	Gln	Thr	Leu	Ala 380	Lys	Glu	Lys	Leu
	Lys	Asp	Phe	Lys	Gly	Lys	Ser	Val	Gly	Tyr	Val	Ser	Pro	Asn	Phe	Glv
	385					390					395					400
<b>5</b> 0 '					405			Gln		410					415	
50	Thr	Leu	Phe	Asn 420	Arg	Gln	Glu	Lys	Lys 425	Gly	Phe	Val	Thr	Ile 430	Gly	Asn
	Lys	Val	Val 435	Leu	Tyr	Gln	Ile	Thr 440		Gln	Asn	Phe	Asn 445	His	Pro	Phe
55	Ser	Ala 450		Glu	Asn			Met	Gln	Arg	Leu		Asn	Asn	Thr	Lys
<i></i>		4 J U					455					460				

Thr Asp Phe Phe Asp Lys Ala Leu Ile Glu Glu Leu Lys Lys Arg Tyr 470 475 Lys Ile Val Lys Tyr Ile Gln 485

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- (2) INFORMATION FOR SEQ ID NO:139:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 142 amino acids
- 10 (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
- 15 (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Helicobacter pylori
- 20 (ix) FEATURE:
  - (A) NAME/KEY: misc feature
  - (B) LOCATION 1...142
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:139:

Met Lys Thr Asn Phe Tyr Lys Ile Lys Leu Leu Phe Ala Trp Cys Leu 10

Ile Ile Gly Met Phe Asn Ala Pro Leu Asn Ala Asp Gln Asn Thr Asp

25

30 Ile Lys Asp Ile Ser Pro Glu Asp Met Ala Leu Asn Ser Val Gly Leu 40

Val Ser Arg Asp Gln Leu Lys Ile Glu Ile Pro Lys Glu Thr Leu Glu 55

Gln Lys Val Ala Ile Leu Asn Asp Tyr Asn Asp Lys Asn Val Asn Ile 35 70 75

Lys Phe Asp Asp Ile Ser Leu Gly Ser Phe Gln Pro Asn Asp Asn Leu 90

Gly Ile Asn Ala Met Trp Gly Ile Gln Asn Leu Leu Met Ser Gln Met 105 110

40 Met Ser Asn Tyr Gly Pro Asn Asn Ser Phe Met Tyr Gly Tyr Ala Pro 120 125

Thr Tyr Ser Asp Ser Ser Phe Leu Pro Pro Ile Leu Gly Tyr

- 45 (2) INFORMATION FOR SEQ ID NO:140:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 208 amino acids
    - (B) TYPE: amino acid
- 50 (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES

#### (ix) FEATURE:

5 (A) N

- (A) NAME/KEY: misc_feature
- (B) LOCATION 1...208
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:
- Leu Ile Asn Asn Asn Asn Asn Lys Lys Leu Arg Gly Phe Phe Leu 10 Lys Val Leu Leu Ser Leu Val Val Phe Ser Ser Tyr Gly Ser Ala Asn Asp Asp Lys Glu Ala Lys Glu Ala Leu Glu Lys Glu Lys Asn Thr 15 Pro Asn Gly Leu Val Tyr Thr Asn Leu Asp Phe Asp Ser Phe Lys Ala Thr Ile Lys Asn Leu Lys Asp Lys Lys Val Thr Phe Lys Glu Val Asn 75 Pro Asp Ile Ile Lys Asp Glu Val Phe Asp Phe Val Ile Val Asn Arg 90 Val Leu Lys Lys Ile Lys Asp Leu Lys His Tyr Asp Pro Val Ile Glu 105 Lys Ile Phe Asp Glu Lys Gly Lys Glu Met Gly Leu Asn Val Glu Leu 25 120 Gln Ile Asn Pro Glu Val Lys Asp Phe Phe Thr Phe Lys Ser Ile Ser 135 Thr Thr Asn Lys Gln Arg Cys Phe Leu Ser Leu His Gly Glu Thr Arg 150 155 30 Glu Ile Leu Cys Asp Asp Lys Leu Tyr Asn Val Leu Leu Ala Val Phe 170 Asn Ser Tyr Asp Pro Asn Asp Leu Leu Lys His Ile Ser Thr Ile Glu 185 Ser Leu Lys Lys Ile Phe Tyr Thr Ile Thr Cys Glu Ala Val Tyr Leu 35 200
  - (2) INFORMATION FOR SEQ ID NO:141:
    - (i) SEQUENCE CHARACTERISTICS:
      - (A) LENGTH: 245 amino acids
      - (B) TYPE: amino acid
      - (D) TOPOLOGY: linear
      - (ii) MOLECULE TYPE: protein
- 45 (iii) HYPOTHETICAL: YES
  - .
- (ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION 1...245
- 55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:141:

Met Ala Gly Thr Gln Ala Ile Tyr Glu Ser Ser Ala Gly Phe Leu Ser Gln Val Ser Ser Ile Ile Ser Ser Thr Ser Gly Val Ala Gly Pro Phe Ala Gly Ile Val Ala Gly Ala Met Thr Ala Ala Ile Ile Pro Ile 40 Val Val Gly Phe Thr Asn Pro Gln Met Thr Ala Ile Met Thr Gln Tyr 55 Asn Gln Ser Ile Ala Glu Ala Val Ser Val Pro Met Lys Ala Ala Asn 10 70 75 Gln Gln Tyr Asn Gln Leu Tyr Gln Gly Phe Asn Asp Gln Ser Met Ala 90 Val Gly Asn Asn Ile Leu Asn Ile Ser Lys Leu Thr Gly Glu Phe Asn 15 105 Ala Gln Gly Asn Thr Gln Ser Ala Gln Ile Ser Ala Val Asn Ser Gln 120 Ile Ala Ser Ile Leu Ala Ser Asn Thr Thr Pro Lys Asn Pro Ser Ala 135 140 20 Ile Glu Ala Tyr Ala Thr Asn Gln Ile Ala Val Pro Ser Val Pro Thr 150 155 Thr Val Glu Met Met Ser Gly Ile Leu Gly Asn Ile Thr Ser Ala Ala 165 170 Pro Lys Tyr Ala Leu Ala Leu Gln Glu Gln Leu Arg Ser Gln Ala Ser 25 180 185 Asn Ser Ser Met Asn Asp Thr Ala Asp Ser Leu Asp Ser Cys Thr Ala 200 Leu Gly Ala Leu Val Gly Ser Ser Lys Val Phe Phe Ser Cys Met Gln 215 220 30 Ile Ser Met Thr Pro Met Ser Val Ser Met Pro Thr Val Met Pro Asn 235 Thr Ser Gly Cys His (2) INFORMATION FOR SEQ ID NO:142: 35

- - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 367 amino acids
    - (B) TYPE: amino acid
- 40 (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:

45

- (A) NAME/KEY: misc feature
- (B) LOCATION 1...367
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:142:
- 55 Met Ile Lys Ser Val Glu Ile Glu Asn Tyr Lys Asn Phe Glu His Leu

	1				5					10					15	
				20		Lys			25	Phe				30	Asn	
5			35			Leu		40					45			
		50				Asn	55					60				•
10	65		-			Arg 70					75					90
10					85	Gly				90					95	
				100		Thr			105					110		
15	-		115			Asp		120					125			
		T20				Thr	135					140				
20	145					Ser 150					155					160
20					165					170					175	
				180		Met			185					190		
25			195			Glu		200					205			
•		210				Gln	215					220				
30	225					Val 230					235					240
-					245	Lys				250					255	
				260		Met			265					270		
35			2/5			Glu		280					285			
		290				Ala	295					300				
40	305 Asn					Thr 310 Asn					315					320
					325	Glu				330					225	
				340		Ala			345					350		Tyr
<b>1</b> 5			355		-,, -			360	шĄ	grå	Met	GIU	365	Arg	стА	

# (2) INFORMATION FOR SEQ ID NO:143:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 409 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

### (iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

5

#### (ix) FEATURE:

- (A) NAME/KEY: misc_feature
- (B) LOCATION 1...409

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:143:

10		(XI	) SE	OORN	CE D	ESCR	TPTI	ON:	SEQ	ID N	0:14	3:				
	Met 1	Ser	Leu	Ile	Arg 5	Val	Asn	Gly	Glu	Ala 10	Phe	Lys	Leu	Ser	Leu 15	Glu
15	Ser	Leu	Glu	Glu 20	Asp	Pro	Phe	Glu	Thr 25	Lys	Glu	Thr	Leu	Glu 30	Thr	Leu
			Leu 35					40					45		_	
		50	Arg				55					60				
20	65		Pro			70					75					80
			Lys		85					90					95	_
25			Arg	100					105					110		
			Glu 115	•	•			120					125			
30		130	Thr				135					140				
50	145		Leu Leu			150					155					160
			Glu		165					170					175	
35			Leu	180					185					190		
			195 Ile					200					205			
40		210	Asp				215					220				
	225		Phe			230					235					240
<u></u>			His		245					250					255	
45	Val	Leu	Asp	260 Cys	Glu	Phe	Gly	Leu	265 Lys	Ala	His	Ser	Asp	270 Gly	Asp	Ala
	Leu	Leu	275 His	Ala	Val	Ile	Asp	280 Ala	Ile	Leu	Gly	Ala	285 Ile	Lys	Gly	Gly
50		290 Ile	Gly	Glu	Trp		295 Pro	Asp	Asn	Asp	Pro	300 Lys	Tyr	Lys	Asn	Ala
	305 Ser	Ser	Lys	Glu		310 Leu	Lys	Ile	Val		315 Asp	Phe	Ser	Gln		320 Ile
55	Gly	Phe	Glu		325 Leu	Glu	Met	Gly		330 Thr	Ile	Phe	Ser		335 Ile	Pro
55				340	-				345					350		

Lys Ile Thr Pro Tyr Lys Pro Ala Ile Leu Glu Asn Leu Ser Gln Leu 355 360 365

Leu Gly Leu Glu Lys Ser Gln Ile Ser Leu Lys Ala Thr Thr Met Glu 370 375 380

Lys Met Gly Phe Ile Gly Lys Gln Glu Gly Leu Leu Val Gln Ala His 385 390 395 400

Val Ser Met Arg Tyr Lys Gln Lys Leu 405

### 10 (2) INFORMATION FOR SEQ ID NO:144:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 270 amino acids
  - (B) TYPE: amino acid
- 15 (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES

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- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
- (ix) FEATURE:
  - (A) NAME/KEY: misc_feature
    - (B) LOCATION 1...270

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:144:

30 Met Lys Lys Phe Val Ala Leu Gly Leu Leu Ser Ala Val Leu Ser Ser Ser Leu Leu Ala Glu Gly Asp Gly Val Tyr Ile Gly Thr Asn Tyr Gln Leu Gly Gln Ala Arg Leu Asn Ser Asn Ile Tyr Asn Thr Gly Asp Cys 35 40 Thr Gly Ser Val Val Gly Cys Pro Pro Gly Leu Thr Ala Asn Lys His 55 Asn Pro Gly Gly Thr Asn Ile Asn Trp His Ser Lys Tyr Ala Asn Gly 70 75 Ala Leu Asn Gly Phe Gly Leu Asn Val Gly Tyr Lys Lys Phe Phe Gln 40 Phe Lys Ser Leu Asp Met Thr Ser Lys Trp Phe Gly Phe Arg Val Tyr 105 Gly Leu Phe Asp Tyr Gly His Ala Asp Leu Gly Lys Gln Val Tyr Ala 45 120 Pro Asn Lys Ile Gln Leu Asp Met Val Ser Trp Gly Val Gly Ser Asp 135 140 Leu Leu Ala Asp Ile Ile Asp Lys Asp Asn Ala Ser Phe Gly Ile Phe 150 155 Gly Gly Val Ala Ile Gly Gly Asn Thr Trp Lys Ser Ser Ala Ala Asn 50 170 Tyr Trp Lys Glu Gln Ile Ile Glu Ala Lys Gly Pro Asp Val Cys Thr 185 Pro Thr Tyr Cys Asn Pro Asn Ala Pro Tyr Ser Thr Asn Thr Ser Thr 55 200

WO 98/18323 PCT/US97/19575

- 225 -

Val Ala Phe Gln Val Trp Leu Asn Phe Gly Val Arg Ala Asn Ile Tyr
210

Lys His Asn Gly Val Glu Phe Gly Val Arg Val Pro Leu Leu Ile Asn
225

230

235

240

5 Lys Phe Leu Ser Ala Gly Pro Asn Ala Thr Asn Leu Tyr Tyr His Leu
245

250

255

Lys Arg Asp Tyr Ser Leu Tyr Leu Gly Tyr Asn Tyr Thr Phe
260

265

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 438 amino acids
(B) Type: amino acid
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein
- (iii) HYPOTHETICAL: YES

20

25

55

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
- (ix) FEATURE:

195

- (A) NAME/KEY: misc_feature
  - (B) LOCATION 1...438
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:145:
- Met Ala Tyr Lys Pro Asn Lys Lys Leu Lys Glu Leu Arg Glu Gln Pro Asn Leu Phe Ser Ile Leu Asp Lys Gly Asp Val Ala Thr Asn Asn Pro Val Glu Glu Ser Asp Lys Ala Asn Lys Ile Gln Glu Pro Leu Pro 35 Tyr Val Val Lys Thr Gln Ile Asn Lys Ala Ser Met Ile Ser Arg Asp Pro Ile Glu Trp Ala Lys Tyr Leu Ser Phe Glu Lys Arg Val Tyr Lys 75 Asp Asn Ser Lys Glu Asp Val Asn Phe Phe Ala Asn Gly Glu Ile Lys 85 90 Glu Ser Ser Arg Val Tyr Glu Ala Asn Lys Glu Gly Phe Glu Arg Arg 105 Ile Thr Lys Arg Tyr Asp Leu Ile Asp Arg Asn Ile Asp Arg Asn Arg 120 Glu Phe Phe Ile Lys Glu Ile Glu Ile Leu Thr His Thr Asn Ser Leu 135 Lys Glu Leu Lys Glu Gln Gly Leu Glu Ile Gln Leu Thr His His Asn 150 50 Glu Thr His Lys Lys Ala Leu Glu Asn Gly Asn Glu Ile Val Lys Glu 170 Tyr Asp His Leu Lys Asp Ile Tyr Gln Glu Val Glu Arg Thr Lys Asp 185 Gly Gly Leu Val Arg Glu Ile Ile Pro Ser Ile Ser Ser Ala Glu Tyr

								*								
	Phe	Lys 210	Leu	Tyr	Asn	Lys	Leu 215	Pro	Phe	Glu	Ser	Ile 220		Asn	Glu	Asn
	Thr 225	Lys	Leu	Asn	Thr	Asn 230	Asp	Asn	Glu	Glu	Val 235	Lys	Lys	Leu	Glu	Phe
5	Glu	Leu	Ala	Lys	Glu 245		His	Ile	Leu		Leu	Glu	Gln	Gln		240 Leu
	Ser	Ala	Thr	Asn 260		Tyr	Ser	Trp		250 Asp	Lys	Asp	Asp		255 Ala	Asn
10	Phe	Ala	Trp 275		Met	His	Årg	Leu 280	265 Ile	Asn	Glu	Asn			Lys	Glu
10	Asn	His 290		Ser	Ala	Asn	Asn 295		Asn	Lys	Ile		285 Gln	Phe	Phe	Phe
	Asn		Gly	Ser	Ile	Leu		Trp	Thr	Lys	Glu	300 Glu	Gln	Ser	Ala	Ile
15	305					310					315					320
13					325					330					335	Glu
				340					345					350		Val
20			355					360					365			Glu
		370					375					380				Tyr
	Asp 385	Lys	Leu	Val	Ser	Leu	Ser	Ala	Ala	Ile		Gln	Ala	Lys	Glu	Gly
25		Asn	Glu	Arg	Pro	390 Asn	Ser	Ser	Ala		395 Asn	Asn	Asn	Pro		400 Lys
	Asn	Thr	Ile	Glu 420		Asn	Thr	Ser		410 Asn	Ile	Ile	Gln	Asn	415 Asn	Asp
30	Asn	Ile	Ile 435		Gln	Ile			425	٠			-	430		
	(2)	INFO	RMAT	'ION	FOR	SEQ	ID N	TO:14	6:							
35		(i)				ARAC									-	
,,						: 21 amin			acid	ls						
						GY:										
Ю		(ii)	MOL	ECUL	E TY	PE:	prot	ein	•							
	. (	iii)	нур	отне	TICA	L: Y	ES									
		(vi)				URCE		b-								
5			(22	, O.	GPUVI	SM:	uett	CODA	ccer	рут	orı					
		(ix)		) NA	ME/K	EY: ON 1			ture					•	•	-
0.		(xi)	SEQ	UENC	E DE	SCRI	PTIO	N: S	EQ I	D NO	:146	:				
	Met	Gln .	Ala :	Leu :	Lys :	Ser :	Leu :	Leu			Ile '	Thr	Lys			Asn
5	Leu	Gly (	Gly '		5 Leu 1	Met 1	His	Ile .	Ala	10 Ile :	Phe :	Ile	Ile	Phe	15 Ile	Trp

	Ile	Gly	Gly	Leu	Lys	Phe	Val	Pro	Tyr	Glu	Ala	Glu	Gly	Ile	Ala	Pro
	D1	••- 1	35	_		_		40	_				45			
	Pne	va. 50	AIA	ASN	ser	Pro	Pne 55	Phe	Ser	Phe	Met		Lys	Phe	Glu	Lys
5	Pro			Lvs	Gln	His		Met	Ser	Glu	Ser	60 Gln	Ser	Met	Gln	Glu.
	65		-2-	-1-		70	-,-				75	<b>5</b> 211	Der	MEC	GIII	80
	Glu	Met	Gln	Asp	Asn	Pro	Lys	Ile	Val	Glu	Asn	Lys	Glu	Trp	His	Lys
					85					90					95	
10	Glu	Asn	Arg			Leu	Val	Ala		Gly	Leu	Gly	Ile	Thr	Ile	Met
10	Tla	Lou	G111	100		37-3	T	7	105	•	<b></b>			110		
	116	neu	115	TIE	neu	vai	ьеп	Leu 120	GIY	ren	rrp	Met	Pro 125	Leu	Met	Gly
	Val	Val		Gly	Leu	Leu	Val	Ala	Glv	Met	Thr	Tle		Thr	T.em	Ser
	•	130	•				135		3			140				501
15	Phe	Leu	Phe	Thr	Thr	Pro	Glu	Val	Phe	Val	Asn	Gln	His	Phe	Pro	Trp.
	145					150					155	•				160
	Leu	Ser	Gly	Ala		Arg	Leu	Val	Val		Asp	Leu	Ala	Leu		Ala
	Glv.	G) v	T.011	Dhe	165	אן א	Glar	Phe	7	170	*	<b>3</b>	m	•	175	~1
20	<b>41</b>	O ₂ y		180	Val	, a	Gry	FIIG	185	Ald	гув	Arg	TYE	190	GIU	GIY
	Lys	Gly	Phe		Leu	Met	Asp	Arg		Ser	Val	Glv	Ile		Thr	Lvs
	-,	-	195	-			-	200				1	205	-1-		-1-
•	Cys		Ser	Gly	Cys	Cys.										
25		210					215									
. 23	(2)	TNFC	רבאקר	מחדי	FOR	SEO	ו מד	NO:14	17.							
					- 01.	226	10 .									
		(i)	SEC	QUENC	E CF	LARAC	TER	ISTIC	CS:							
20								se pa								
30								acio								
								douk ular								
*			,_	,, 10	FOLC	<i>G</i> 1:	CIIC	urai	•							
		(ii)	MOI	ECUI	E TY	PE:	DNA	(ger	omic	:)						
35																
	, (	iii)	HYE	POTHE	TICA	T: N	O									
		(4)	דינג ת	'I-SE	MCE.	MO										
		(14)	MIAT	. I - DE	MOE:	NO										
40		(vi)	ORI	GINA	L SC	URCE	:		•							
								.coba	cter	pyl	.ori			•		
		(ix)		TURE		-		_			•					
45				l) NA l) LO				_fea	ture	:						
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		(xi)	SEQ	UENC	E DE	SCRI	PTIC	N: S	EO T	סוא ס	. 147					

TATACCATGG TGGGCGCTAA

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(2) INFORMATION FOR SEQ ID NO:148:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23 base pairs

(B) TYPE: nucleic acid

	(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
5	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
10	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
15	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 123</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:148:	
20	ATGAATTCGA GTAAGGATTT TTG	23
25	(2) INFORMATION FOR SEQ ID NO:149:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double	
30	(D) TOPOLOGY: circular  (ii) MOLECULE TYPE: DNA (genomic)  (iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
35	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>	
÷.	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature</pre>	
40	(B) LOCATION 122	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:149:	
45	TTAACCATGG TGAAAAGCGA TA	22
	(2) INFORMATION FOR SEQ ID NO:150:	
50	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
55	(ii) MOLECULE TYPE: DNA (genomic)	

	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
5	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	·
10	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 123	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:150:	
15	TAGAATTC	GC ATAACGATCA ATC	23
13	(2) INFO	RMATION FOR SEQ ID NO:151:	
20	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
25	(ii)	MOLECULE TYPE: DNA (genomic)	
	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
30	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
35 .	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 122	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:151:	
40		GG TGAGTTTGAT GA  ORMATION FOR SEQ ID NO:152:	22
45	(1)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	÷
50	(ii)	MOLECULE TYPE: DNA (genomic)	
	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
55	1-025	ORIGINAL COMMON	

	(A) ORGANISM: Helicobacter pylori	
5	(ix) FEATURE:  (A) NAME/KEY: misc_feature  (B) LOCATION 125	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:152:	
10	ATGAATTCAA TTTTTTATTT TGCCA	25
10	(2) INFORMATION FOR SEQ ID NO:153:	
15	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 21 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
20	(ii) MOLECULE TYPE: DNA (genomic)	
20	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
25	(vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori	
30	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 121</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:153:	
35	AATTCCATGG TGGGGGCTAT G	1
	(2) INFORMATION FOR SEQ ID NO:154:	
40	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
.45	(ii) MOLECULE TYPE: DNA (genomic)	
. 43	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
50	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
55	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 123</pre>	

	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:154:	
<b>5</b>	ATGAATTC	TTC GATAGCCAAA ATC	23
5	(2) INFO	DRMATION FOR SEQ ID NO:155:	
10	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
15	(ii)	MOLECULE TYPE: DNA (genomic)	•
	.(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
20	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
25	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 125	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:155:	
20	AATTCCAT	TGG TGCATAACTT CCATT	25
30	(2) INFO	DRMATION FOR SEQ ID NO:156:	
35	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
40		MOLECULE TYPE: DNA (genomic)	
	(iii)	HYPOTHETICAL: NO	
•	(iv)	ANTI-SENSE: NO	
45	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
50	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 125	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:156:	

	(2) INFOR	MATION FOR SEQ ID NO:157:				
5	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 24 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular				
10	(ii)	MOLECULE TYPE: DNA (genomic)				
	(iii)	HYPOTHETICAL: NO		•		
	(iv)	ANTI-SENSE: NO				
15	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter	pylori			
	(ix)	FEATURE:				
20		(A) NAME/KEY: misc_feature (B) LOCATION 124				
	(xi)	SEQUENCE DESCRIPTION: SEQ ID	NO:157:			
25	ATTTCCATG	G TCATGTCTCA TATT	•			2
	(2) INFOR	MATION FOR SEQ ID NO:158:		4		
30	(i) :	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular				
35	(ii) !	MOLECULE TYPE: DNA (genomic)				
	(iii) 1	HYPOTHETICAL: NO				
	(iv) 1	ANTI-SENSE: NO				
40	(vi) (	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter	pylori		•	
	(ix) I	FEATURE:		٠		
45		(A) NAME/KEY: misc_feature (B) LOCATION 123		•		
	(xi) S	SEQUENCE DESCRIPTION: SEQ ID	NO:158:		,	
50	ATGAATTCC	A TCTTTATTC CAC				23
	(2) INFORM	MATION FOR SEQ ID NO:159:				
	(i) s	EQUENCE CHARACTERISTICS: (A) LENGTH: 27 base pairs				
55		(B) (WO)				

		(C) STRANDEDNESS: double (D) TOPOLOGY: circular			•
5	(ii)	MOLECULE TYPE: DNA (genomic)			•
3	(iii)	HYPOTHETICAL: NO			•
	(iv)	ANTI-SENSE: NO	•	•	•
10	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori			
15	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 127			
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:15	9:		
20	ÄACCATGG	TG ATTTTAAGCA TTGAAAG			2
	(2) INFO	RMATION FOR SEQ ID NO:160:			•
25	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 28 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular			
30		MOLECULE TYPE: DNA (genomic)			
		HYPOTHETICAL: NO			
35		ANTI-SENSE: NO  ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori			•
40	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 128			
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:16	):		
45	AAGAATTC	CA CTCAAAATTT TTTAACAG	;		28
43	(2) INFO	RMATION FOR SEQ ID NO:161:			
50	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular			
55	(ii)	MOLECULE TYPE: DNA (genomic)			

	(iii)	HYPOTHETICAL: NO	•	
٠,	(iv)	ANTI-SENSE: NO		
5	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
10	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 125		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:161:		
15	GATCATCC	AT ATGTTATCTT CTAAT		2
	(2) INFO	RMATION FOR SEQ ID NO:162:		
20	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		- A
25	(ii)	MOLECULE TYPE: DNA (genomic)		
	(iii)	HYPOTHETICAL: NO		
30	•	ANTI-SENSE: NO ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
35	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 123		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:162:		
40	• .	AC CATTTTAACC CTG RMATION FOR SEQ ID NO:163:		2:
		SEQUENCE CHARACTERISTICS:	· ·	
45		<ul><li>(A) LENGTH: 27 base pairs</li><li>(B) TYPE: nucleic acid</li><li>(C) STRANDEDNESS: double</li><li>(D) TOPOLOGY: circular</li></ul>		
50	(ii)	MOLECULE TYPE: DNA (genomic)		
	(iii)	HYPOTHETICAL: NO		

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

		(A) ORGANISM: Helicobacter pylori	•	
5	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 127		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:163:		٠
10	TATACCAT	GG TGAAATTTT TCTTTTA		27
.10	(2) INFO	RMATION FOR SEQ ID NO:164:		
15	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		
20	(ii)	MOLECULE TYPE: DNA (genomic)		
20	(iii)	HYPOTHETICAL: NO	•	
	(iv)	ANTI-SENSE: NO		
25	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
30	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 125		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:164:		
35	AGAATTCA	AT TGCGTCTTGT AAAAG		25
	(2) INFO	RMATION FOR SEQ ID NO:165:	·	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 24 base pairs		
40		(B) TYPE: nucleic acid (C) STRANDEDNESS: double	· · · · · · · · · · · · · · · · · · ·	
		(D) TOPOLOGY: circular		
45	(ii)	MOLECULE TYPE: DNA (genomic)		
	(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO		
50	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
	(ix)	FEATURE: (A) NAME/KEY: misc_feature		
55		(B) LOCATION 124		

	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:165:	
5	TATACCATGG TGATGGACAA ACTC	24
	(2) INFORMATION FOR SEQ ID NO:166:	
10	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	·
15	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
<b>30</b>	(iv) ANTI-SENSE: NO	
20	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
25	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 123</pre>	· · · · · · · · · · · · · · · · · · ·
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:166:	
30	ATGAATTCCC ACTTGGGGCG ATA	23
	(2) INFORMATION FOR SEQ ID NO:167:	
35	<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 25 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: double</li> <li>(D) TOPOLOGY: circular</li> </ul>	
40	(ii) MOLECULE TYPE: DNA (genomic)	``
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
45	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>	
50	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 125</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:167:	•
55	TTATGGATCC AAACCAATTA AAACT	25

*	(2) INFORMAT	TION FOR SEQ	ID NO:168:					
		QUENCE CHARAC						
5		) TYPE: nucl	-					
		) STRANDEDNE		•				
		) TOPOLOGY:				٠.		
		•						
	(ii) MOL	ECULE TYPE:	DNA (genomie	<b>=</b> )				
10								
	(iii) HYP	OTHETICAL: N	10					
	/ \	T CENTER NO				,	•	
	(IV) ANI	'I-SENSE: NO						
15	(vi) ORT	GINAL SOURCE	!•					
••		ORGANISM:		r pylori	•			
				Pyrorr				
	(ix) FEA	TURE:			•			
	(A	) NAME/KEY:	misc_feature	2				
20	. (B	) LOCATION 1	23					
	(xi) SEQ	UENCE DESCRI	PTION: SEQ	ID NO:168:				
			-					
25	TATCTCGAGT	'ATAGAGAAG GG	iC .					23
23	(2) INFORMAT	ION FOR SEQ	TD NO.169.					
	(2) INI ORBI	TON TON DEQ	10.103.					
	(i) SEQ	UENCE CHARAC	TERISTICS:	•				
		) LENGTH: 22		•				
30		) TYPE: nucl						
		) STRANDEDNE						
	(D	) TOPOLOGY:	circular					
	(22) MOT	7077 P 0000						
35	(11) MOL	ECULE TYPE:	DNA (genomic	<b>:</b> )				
33	(iii) HVD	OTHETICAL: N	· O			•	•	
	(111) 1111	oimiican. N						
	(iv) ANT	I-SENSE: NO			•			
40	(vi) ORI	GINAL SOURCE	:	•		·	•	
	(A	) ORGANISM:	Helicobacter	pylori				
			•					
	(ix) FEA				·			
45		) NAME/KEY:		•				
43	(B	) LOCATION 1	., 22			*		
	(ri) SEO	UENCE DESCRI	בי בער זיים	'D NO.169.		•		
	(7.17) 550	omice proces	riion. SEQ 1	.D NO:169:		•		
	TTAACCATGG TO	GAAAAGCGA TA						22
50								
	(2) INFORMAT	ION FOR SEQ	ID NO:170:					
					,			
		UENCE CHARAC						
E E		) LENGTH: 24						
55	(B)	) TYPE: nucl	eıc acid					

	(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
5	(ii) MOLECULE TYPE: DNA (genomic)	
,	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
10	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
15	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 124</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:170:	
20	TAGAATTCGC CTCTAAAACT TTAG	2
	(2) INFORMATION FOR SEQ ID NO:171:	
25	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
30	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
35	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
<b>1</b> 0	(ix) FEATURE:  (A) NAME/KEY: misc_feature  (B) LOCATION 122	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:171:	
15	TTAACCATGG TGAAAAGCGA TA	2:
٠.	(2) INFORMATION FOR SEQ ID NO:172:	
50	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
	(ii) MOLECULE TYPE: DNA (genomic)	

	(iii)	HYPOTHETICAL: NO			
	(iv)	ANTI-SENSE: NO			
5	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori			
10	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 123			
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:172:			
15	TAGAATTC	GC ATAACGATCA ATC	•		23
13	(2) INFO	RMATION FOR SEQ ID NO:173:		•	•
20	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		.*	
25		MOLECULE TYPE: DNA (genomic) HYPOTHETICAL: NO			
		ANTI-SENSE: NO			
30	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori			
35	(ix)	<pre>FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 122</pre>			
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:173:		÷	
40	ATATCCAT	GG TGAGTTTGAT GA			22
	(2) INFO	RMATION FOR SEQ ID NO:174:			
45	( <b>i</b> )	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	· .		
50	(ii)	MOLECULE TYPE: DNA (genomic)			
	(iii)	HYPOTHETICAL: NO		•	
	(iv)	ANTI-SENSE: NO			•
55	10023	ORIGINAL COMPORT			

	·	(A) ORGANISM: Helicobacter pylori
5	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 125
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:174:
10	ATGAATTC	AA TTTTTATTT TGCCA
10	(2) INFO	RMATION FOR SEQ ID NO:175:
15	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular
20	(ii)	MOLECULE TYPE: DNA (genomic)
20	(iii)	HYPOTHETICAL: NO
	(iv)	ANTI-SENSE: NO
25	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori
30	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 123
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:175:
- 35	AATTCCAT	GG CTATCCAAAT CCG
	(2) INFO	RMATION FOR SEQ ID NO:176:
40	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular
45	(ii)	MOLECULE TYPE: DNA (genomic)
, <del>1</del> 3	(iii)	HYPOTHETICAL: NO
	(iv)	ANTI-SENSE: NO
50	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori
55	(ix)	FEATURE:  (A) NAME/KEY: misc_feature  (B) LOCATION 125

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	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:176:	
5	ATGAATTC	GC CAAAATCGTA GTATT	25
,	(2) INFO	RMATION FOR SEQ ID NO:177:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 24 base pairs	
10		(B) TYPE: nucleic acid	
10		(C) STRANDEDNESS: double	
	•	(D) TOPOLOGY: circular	
15	(ii)	MOLECULE TYPE: DNA (genomic)	
13	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
20	(vi)	ORIGINAL SOURCE:	
	. (,	(A) ORGANISM: Helicobacter pylori	
	(ix)	FEATURE:	
		(A) NAME/KEY: misc_feature	
25		(B) LOCATION 124	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:177:	
30	GATACCAT	GG AATTTATGAA AAAG	24
50	(2) INFO	RMATION FOR SEQ ID NO:178:	
	(i)	SEQUENCE CHARACTERISTICS:	
		(A) LENGTH: 25 base pairs	
35		(B) TYPE: nucleic acid	
		(C) STRANDEDNESS: double	
		(D) TOPOLOGY: circular	
40	(ii)	MOLECULE TYPE: DNA (genomic)	
	′ (iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
45	(vi)	ORIGINAL SOURCE:	
		(A) ORGANISM: Helicobacter pylori	
	(ix)	FEATURE:	
50		(A) NAME/KEY: misc_feature (B) LOCATION 125	
	(vi)	SEQUENCE DESCRIPTION: SEQ ID NO:178:	
	(54)		

55

	(2) INFO	RMATION FOR SEQ ID NO:179:		
5	<b>(i)</b>	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 19 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		
10	(ii)	MOLECULE TYPE: DNA (genomic)	•	
	(iii)	HYPOTHETICAL: NO	· ,	
.•	(iv)	ANTI-SENSE: NO		
15	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		<b>.</b>
20	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 119		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:179:		
25		TT TAGAAATCG RMATION FOR SEQ ID NO:180:		. 1
30	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 20 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		
35	(ii)	MOLECULE TYPE: DNA (genomic)		
	(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO		
40	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
45	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 120		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:180:		•
50	ATTTCAACC	A ATTCAATGCG		20
	(2) INFOR	MATION FOR SEQ ID NO:181:		
55	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid		

•		(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
5	(ii)	MOLECULE TYPE: DNA (genomic)	
J	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
10	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
15	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 120	-
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:181:	
20	GCCCCTTT	TG ATTTGAAGCT	20
	(2) INFO	RMATION FOR SEQ ID NO:182:	
25	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double	
30		(D) TOPOLOGY: circular  MOLECULE TYPE: DNA (genomic)	
		HYPOTHETICAL: NO	
35	-	ANTI-SENSE: NO ORIGINAL SOURCE:	
		(A) ORGANISM: Helicobacter pylori	
40	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 122	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:182:	
45	TCGCTCCA	AG ATACCAAGAA GT	. 22
	(2) INFO	RMATION FOR SEQ ID NO:183:	
50	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
55	(ii)	MOLECULE TYPE: DNA (genomic)	

	(iii)	HYPOTHETICAL: NO	:	
	(iv)	ANTI-SENSE: NO		
5	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
	· (iv)	FEATURE:		
10	(13.)	(A) NAME/KEY: misc_feature (B) LOCATION 122		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:183	: · · ·	
15	CTTGAATT	AG GGGCAAAGAT CG		22
13	(2) INFO	ORMATION FOR SEQ ID NO:184:		
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 22 base pairs		• •
20		(B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular	•	
	(ii)	MOLECULE TYPE: DNA (genomic)		
25	•	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO	•	
30	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
35	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 122		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:184	:	
40	ATGCGTTT	TT ACCCAAAGAA GT	•	22
	(2) INFO	RMATION FOR SEQ ID NO:185:		
<b>15</b>	<b>(i)</b>	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double		
	/551	(D) TOPOLOGY: circular		
50	•	MOLECULE TYPE: DNA (genomic) HYPOTHETICAL: NO		
		ANTI-SENSE: NO	, · ·	
55		ORIGINAL SOURCE:	÷	

•		(A) ORGANISM: Helicobacter pylori	•	•
	(ix)	FEATURE:		
5		(A) NAME/KEY: misc_feature (B) LOCATION 122		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:185:		
10	ATAACGCC	AC TTCCTTATTG GT		22
	(2) INFO	RMATION FOR SEQ ID NO:186:		
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 19 base pairs		
15		(B) TYPE: nucleic acid		
		(C) STRANDEDNESS: double		
		(D) TOPOLOGY: circular	•	•
20	(ii)	MOLECULE TYPE: DNA (genomic)		
	(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO		
25	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
	(ix)	FEATURE:		
30	•	(A) NAME/KEY: misc_feature (B) LOCATION 119		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:186:	•	
35	CTTTGGGT	AA AAACGCATC		19
	(2) INFO	RMATION FOR SEQ ID NO:187:		
	(i)	SEQUENCE CHARACTERISTICS:		
10		(A) LENGTH: 20 base pairs (B) TYPE: nucleic acid		
. •		(C) STRANDEDNESS: double		
		(D) TOPOLOGY: circular		
15	(ii)	MOLECULE TYPE: DNA (genomic)		
	(iii)	HYPOTHETICAL: NO	•	
	(iv)	ANTI-SENSE: NO		
0	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	· ·	
	(ix)	FEATURE:		•
5		(A) NAME/KEY: misc_feature		

	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:187:		
5	CGATCTTT	GA TCCTAATTCA		20
`	(2) INFO	RMATION FOR SEQ ID NO:188:		
	(i)	SEQUENCE CHARACTERISTICS:		
10		<ul><li>(A) LENGTH: 19 base pairs</li><li>(B) TYPE: nucleic acid</li><li>(C) STRANDEDNESS: double</li></ul>		
		(D) TOPOLOGY: circular		
15	(ii)	MOLECULE TYPE: DNA (genomic)		
	: (iii)	HYPOTHETICAL: NO		٠
	(iv)	ANTI-SENSE: NO		,
20	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
25	(ix)	FEATURE: (A) NAME/KEY: misc_feature		
23	(vi)	(B) LOCATION 119		
		SEQUENCE DESCRIPTION: SEQ ID NO:188:		•
30		GC CTATGCTGA		19
		RMATION FOR SEQ ID NO:189:		
35	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid		
-		(C) STRANDEDNESS: double (D) TOPOLOGY: circular		
40	(ii)	MOLECULE TYPE: DNA (genomic)	•	
	(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO		
45 .	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
50	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 122		1
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:189:		

	(2) INFORMATION FOR SEQ ID NO:190:	
5	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
10	(ii) MOLECULE TYPE: DNA (genomic)	
-	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
15	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>	
20	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 123</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:190:	
25	GGATTATGCG ATTGTTTTAC AAG (2) INFORMATION FOR SEQ ID NO:191:	
30	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 21 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
35	(ii) MOLECULE TYPE: DNA (genomic)	•
	(iii) HYPOTHETICAL: NO	
40	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori	
45	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 121</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:191:	
50	GTCTTTAGCA AAAATGGCGT C	2:
J <b>U</b>	(2) INFORMATION FOR SEQ ID NO:192:	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 21 base pairs	·
55	(B) TYPE: nucleic acid	

		(C) STRANDEDNESS: double	
,		(D) TOPOLOGY: circular	
5	(ii)	MOLECULE TYPE: DNA (genomic)	
	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
10	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
	(ix)	FEATURE:	
15		(A) NAME/KEY: misc_feature (B) LOCATION 121	
:	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:192:	
20	AATGAGCG	TA AGAGAGCCTT C	21
	(2) INFO	DRMATION FOR SEQ ID NO:193:	
25	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 18 base pairs	
		(B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular	
30	(ii)	MOLECULE TYPE: DNA (genomic)	
	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
35	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
٠.	(ix)	FEATURE:	
40		(A) NAME/KEY: misc_feature (B) LOCATION 118	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:193:	
45	CTTATGGGG	GG TATTGTCA	18
	(2) INFO	RMATION FOR SEQ ID NO:194:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 18 base pairs	,
50		(B) TYPE: nucleic acid	
		(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
55	(ii)	MOLECULE TYPE: DNA (genomic)	

	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
5	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
10	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 118	
•	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:194:	
15	AGCATGTG	GG TATCCAGC	18
	(2) INFO	RMATION FOR SEQ ID NO:195:	
20	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 19 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
25	(ii)	MOLECULE TYPE: DNA (genomic)	
	(iii)	HYPOTHETICAL: NO	
30		ANTI-SENSE: NO ORIGINAL SOURCE:	
		(A) ORGANISM: Helicobacter pylori	
35	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 119	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:195:	
40	•	GC CTAAAGACT	19
45		RMATION FOR SEQ ID NO:196:  SEQUENCE CHARACTERISTICS:  (A) LENGTH: 18 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
50	(ii)	MOLECULE TYPE: DNA (genomic)	• .
. 50	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
55	(vi)	ORIGINAL SOURCE:	

		(A) ORGANISM: Helicobacter pylori		•	
	(32)	FEATURE:	•		
	(12)	(A) NAME/KEY: misc_feature	•	•	
5		(B) LOCATION 118			
•		(b) Docation 1.1.10			
*	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:196:			
	CTGCCTCC	AC CTTTGATC			
10					18
	(2) INFO	RMATION FOR SEQ ID NO:197:			
	(i)	SEQUENCE CHARACTERISTICS:			
		(A) LENGTH: 19 base pairs			
15		(B) TYPE: nucleic acid			
•		(C) STRANDEDNESS: double			
		(D) TOPOLOGY: circular			
	(ii)	MOLECULE TYPE: DNA (genomic)			
20				•	
	(iii)	HYPOTHETICAL: NO			
	(iv)	ANTI-SENSE: NO			
25					
23	(V1)	ORIGINAL SOURCE:			
		(A) ORGANISM: Helicobacter pylori			
	(:)	LYDA MITO D			
	(1x)	FEATURE:			
30		(A) NAME/KEY: misc_feature (B) LOCATION 119			
50		(B) LOCATION 119			
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:197:			
25	ACCAATAT	CA ATTGGCACT			19
35					
	(2) INFO	RMATION FOR SEQ ID NO:198:			
	(2)	CHAVENOR CUSTS COMPANIES	•		
	(1)	SEQUENCE CHARACTERISTICS:			
40		(A) LENGTH: 18 base pairs			
7U .		(B) TYPE: nucleic acid			
		(C) STRANDEDNESS: double			
		(D) TOPOLOGY: circular			
	(11)	MOLECULE TYPE: DNA (genomic)			
45	,,	DIA (genomic)			
	(iii)	HYPOTHETICAL: NO		•	
	,,		÷	•	
	(iv)	ANTI-SENSE: NO			
			·		
50	(vi)	ORIGINAL SOURCE:			
		(A) ORGANISM: Helicobacter pylori			
		* • · · · · · · · · · · · · · · · · · ·			
	(ix)	FEATURE:	•		
		<pre>(A) NAME/KEY: misc_feature</pre>			
55		(B) LOCATION 118			

	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:198:	
5	ACTTGGAAAA GCTCTGCA	18
ی	(2) INFORMATION FOR SEQ ID NO:199:	
10	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 19 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
15	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO  (iv) ANTI-SENSE: NO	
20	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
25	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 119</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:199:	
30	CTTGCTTGTC ATATCTAGC	19
	(2) INFORMATION FOR SEQ ID NO:200:  (i) SEQUENCE CHARACTERISTICS:	
35	(A) LENGTH: 18 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular	
40	(ii) MOLECULE TYPE: DNA (genomic)	
,10	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
45	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
50	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 118</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:200:	
55	GTTGAAGTGT TGGTGCTA	- 18

	(2) INFORMATION FOR SEQ ID NO:201:		
5	<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 22 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: double</li> <li>(D) TOPOLOGY: circular</li> </ul>		
10	(ii) MOLECULE TYPE: DNA (genomic)		
	(iii) HYPOTHETICAL: NO		•
	(iv) ANTI-SENSE: NO	· ·	•
15	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>		
20	<pre>(ix) FEATURE:      (A) NAME/KEY: misc_feature      (B) LOCATION 122</pre>		
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:201:		
25	CAAGCAAGTG GTTTGGTTTT AG (2) INFORMATION FOR SEQ ID NO:202:		2:
30	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		· .
35	(ii) MOLECULE TYPE: DNA (genomic)		
	(iii) HYPOTHETICAL: NO		
40	(iv) ANTI-SENSE: NO		
40	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>		
45	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 122</pre>		
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:202:		
50	TGGAAAGAGC AAATCATTGA AG	·	22
	(2) INFORMATION FOR SEQ ID NO:203:		
55	<ul><li>(i) SEQUENCE CHARACTERISTICS:</li><li>(A) LENGTH: 21 base pairs</li><li>(B) TYPE: nucleic acid</li></ul>		

	(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
· -	(ii) MOLECULE TYPE: DNA (genomic)	
5	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
10	(vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori	
15	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 121</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:203:	
20	GCCCATAATC AAAAAGCCCA T	2:
	(2) INFORMATION FOR SEQ ID NO:204:	
<b>25</b> ²	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 24 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: doublé  (D) TOPOLOGY: circular	
30	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
25	(iv) ANTI-SENSE: NO	
35	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>	
-	<pre>(ix) FEATURE:     (A) NAME/KEY: misc feature</pre>	
40	(B) LOCATION 124	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:204:	
45	CTAAAACCAA ACCACTTGCT TGTC	24
	(2) INFORMATION FOR SEQ ID NO:205:	
50	<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 16 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: double</li> <li>(D) TOPOLOGY: circular</li> </ul>	
55	(ii) MOLECULE TYPE: DNA (genomic)	

**55** .

(vi) ORIGINAL SOURCE:

	(iii) HYI	POTHETICAL: NO				
	(iv) ANT	'I-SENSE: NO	•			
5		GINAL SOURCE: .) ORGANISM: Helicob	acter pylori			
10	(ix) FE <i>I</i> ( <i>I</i> (E	TURE:  NAME/KEY: misc_fe  LOCATION 116	ature			
	(xi) SEQ	UENCE DESCRIPTION:	SEQ ID NO:205:	•		
15	GTAAAACGAC G	GCCAG ION FOR SEQ ID NO:2	06:		·	16
20	(i) SEÇ (A (E	UENCE CHARACTERISTI ) LENGTH: 17 base p ) TYPE: nucleic aci ) STRANDEDNESS: dou	CS: airs d	·		
	(D	) TOPOLOGY: circula	r			
25		ECULE TYPE: DNA (ge	nomic)			
•		OTHETICAL: NO			·	•
30		I-SENSE: NO GINAL SOURCE:				
		ORGANISM: Helicob	acter pylori			
35	(ix) FEA (A (B	TURE: ) NAME/KEY: misc_fe ) LOCATION 117	ature			
	(xi) SEQ	JENCE DESCRIPTION:	SEQ ID NO:206:			
40	CAGGAAACAG C	FATGAC ION FOR SEQ ID NO:2	07.		٠.	17
45	(i) SEQ	JENCE CHARACTERISTIC LENGTH: 21 base partype: nucleic acid	CS: airs			
	(C	STRANDEDNESS: doubt	ole			
50	•	CULE TYPE: DNA (gen	nomic)			
		THETICAL: NO				
	(iv) ANT	-SENSE: NO				

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(A)	ORGANISM:	Helicobacter	pylori
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### (ix) FEATURE:

- (A) NAME/KEY: misc_feature
- 5 (B) LOCATION 1...21
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:207:

### ATCTTACCTA TCACCTCAAA T

21

(2) INFORMATION FOR SEQ ID NO:208:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 21 base pairs
- 15 (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: double
  - (D) TOPOLOGY: circular
  - (ii) MOLECULE TYPE: DNA (genomic)
    - - (iii) HYPOTHETICAL: NO
  - (iv) ANTI-SENSE: NO
- - (ix) FEATURE:
    - (A) NAME/KEY: misc_feature
- 30 (B) LOCATION 1...21
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:208:

AGACAGCAAC ATCTTTGTGA A

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## **CLAIMS**

- An isolated nucleic acid comprising a nucleotide sequence encoding an
   H. pylori polypeptide at least about 60% homologous to an amino acid sequence selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146.
- An isolated nucleic acid comprising a nucleotide sequence encoding an H. pylori polypeptide selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146.
  - 3. An isolated nucleic acid which encodes an *H. pylori* polypeptide, comprising a nucleotide sequence at least about 60% homologous to a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.
    - 4. The isolated nucleic acid of claim 1, comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.
    - 5. An isolated nucleic acid molecule encoding an *H. pylori* polypeptide, comprising a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising the nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.
    - 6. An isolated nucleic acid comprising a nucleotide sequence of at least 8 nucleotides in length, wherein the sequence hybridizes under stringent hybridization conditions to a nucleic acid having a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.
  - 7. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cell envelope polypeptide or a fragment thereof, said nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, SEQ ID NO: 48, SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID

NO: 11, SEQ ID NO: 71, SEQ ID NO: 17, SEQ ID NO: 57, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 8, and SEQ ID NO: 21, or a complement thereof.

- 8. The isolated nucleic acid of claim 7, wherein said *H. pylori* cell envelope 5 polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, and SEQ ID NO: 48, or a complement thereof.
- The isolated nucleic acid of claim 7, wherein said H. pylori cell envelope
   polypeptide or a fragment thereof is an H. pylori outer membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, and SEQ ID NO: 71, or a complement thereof.
  - 10. The isolated nucleic acid of claim 9, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11 and SEQ ID NO:71, or a complement thereof.
- The isolated nucleic acid of claim 9, wherein said H. pylori outer membrane polypeptide or a fragment thereof is an H. pylori polypeptide having a terminal phenylalanine residue or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, or a complement thereof.
- 12. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cell envelope polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, SEQ ID NO: 121, SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO:

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101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, SEQ ID NO: 130, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, and SEQ ID NO: 94.

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13. The isolated nucleic acid of claim 12, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, and SEQ ID NO: 121.

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14. The isolated nucleic acid of claim 12, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, and SEQ ID NO: 130.

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15. The isolated nucleic acid of claim 14, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof selected from the group consisting of SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, and SEQ ID NO: 84 and SEQ ID NO:144.

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16. The isolated nucleic acid of claim 14, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, and SEQ ID NO: 131.

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17. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* secreted polypeptide or a fragment thereof, said nucleic acid selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 32, SEQ ID NO: 51, SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 22, SEQ ID NO: 29, SEQ

ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 53, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, and SEQ ID NO: 68, or a complement thereof.

18. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* secreted polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 145, SEQ ID NO: 105, SEQ ID NO: 124, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 82, SEQ ID NO: 86, SEQ ID NO: 95, SEQ ID NO: 102, SEQ ID NO: 104, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 122, SEQ ID NO: 126, SEQ ID NO: 132, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, and SEQ ID NO: 141.

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- 19. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cellular polypeptide or a fragment thereof, said nucleic acid selected from the group consisting of SEQ ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 47, SEQ ID NO: 50, SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 69, SEQ ID NO: 70, and SEQ ID NO: 73, or a complement thereof.
- 20. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cellular polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 85, SEQ ID NO: 88, SEQ ID NO: 93, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 120, SEQ ID NO: 123, SEQ ID NO: 133, SEQ ID NO: 137, SEQ ID NO: 142, SEQ ID NO: 143, and SEQ ID NO: 146.
- 21. A probe comprising a nucleotide sequence consisting of at least 8

  30 nucleotides of a nucleotide sequence selected from the group consisting of SEQ ID NO:

  1-SEQ ID NO: 73, or a complement thereof.
- 22. A recombinant expression vector comprising the nucleic acid of any of claims 1, 2, 3, 4, 5, 6, 7, 12, 17, 18, 19 or 20 operably linked to a transcription regulatory element.

- 23. A cell comprising a recombinant expression vector of claim 22.
- 24. A method for producing an *H. pylori* polypeptide comprising culturing a cell of claim 23 under conditions that permit expression of the polypeptide.

- 25. The method of claim 24, further comprising purifying the polypeptide from the cell.
- 26. A method for detecting the presence of a *Helicobacter* nucleic acid in a sample comprising:
  - (a) contacting a sample with a nucleic acid of any of claims 6 or 21 so that a hybrid can form between the probe and a *Helicobacter* nucleic acid in the sample; and
- (b) detecting the hybrid formed in step (a), wherein detection of a hybrid indicates the presence of a *Helicobacter* nucleic acid in the sample.
  - 27. An isolated *H. pylori* polypeptide comprising an amino acid sequence at least about 60% homologous to an *H. pylori* polypeptide selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146.

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28. An isolated *H. pylori* polypeptide which is encoded by a nucleic acid comprising a nucleotide sequence at least about 60% homologous to a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73.

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29. The isolated *H. pylori* polypeptide of claim 28, wherein said polypeptide is encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73.

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- 30. An isolated *H. pylori* polypeptide which is encoded by a nucleic acid which hybridizes under stringent hybridization conditions to a nucleic acid selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.
- 31. An isolated *H. pylori* polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146.

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32. An isolated *H. pylori* cell envelope polypeptide or a fragment thereof, wherein said polypeptide is selected from the group consisting of SEQ ID NO: 76, SEQ

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ID NO: 98, SEQ ID NO: 121, SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, SEQ ID NO: 130, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, and SEQ ID NO: 94.

- 33. The isolated polypeptide of claim 32, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, and SEQ ID NO: 121.
- 34. The isolated polypeptide of claim 32, wherein said *H. pylori* cell
  envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide
  or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID
  NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ
  ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101,
  SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO:
  131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID
  NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, and SEQ ID NO: 130.
  - 35. The isolated polypeptide of claim 34, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof selected from the group consisting of SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, and SEQ ID NO: 84 and SEQ ID NO:144.

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36. The isolated polypeptide of claim 34, wherein said *H. pylori* outer
30 membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a
terminal phenylalanine residue or a fragment thereof selected from the group consisting
of SEQ ID NO: 89, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO:
80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO:
101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, and SEQ
35 ID NO: 131.

37. An isolated *H. pylori* cell envelope polypeptide or a fragment thereof, wherein said polypeptide is encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, SEQ ID NO: 48, SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, SEQ ID NO: 71, SEQ ID NO: 17, SEQ ID NO: 57, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 8, and SEQ ID NO: 21.

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38. The isolated polypeptide of claim 37, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, and SEQ ID NO: 48.

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39. The isolated polypeptide of claim 37, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, and SEQ ID NO: 71.

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40. The isolated polypeptide of claim 39, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11 and SEQ ID NO:71.

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41. The isolated polypeptide of claim 39, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58.

- 42. An isolated *H. pylori* cellular polypeptide or a fragment thereof, wherein said polypeptide is selected from the group consisting of SEQ ID NO: 85, SEQ ID NO: 88, SEQ ID NO: 93, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 120, SEQ ID NO: 123, SEQ ID NO: 133, SEQ ID NO: 137, SEQ ID NO: 142, SEQ ID NO: 143, and SEQ ID NO: 146.
- 43. An isolated *H. pylori* cellular polypeptide or a fragment thereof, wherein said polypeptide is encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 47, SEQ ID NO: 50, SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 69, SEQ ID NO: 70, and SEQ ID NO: 73.
- 44. An isolated *H. pylori* secreted polypeptide or a fragment thereof, wherein said polypeptide is selected from the group consisting of SEQ ID NO: 145, SEQ ID NO: 105, SEQ ID NO: 124, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 82, SEQ ID NO: 86, SEQ ID NO: 95, SEQ ID NO: 102, SEQ ID NO: 104, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 122, SEQ ID NO: 126, SEQ ID NO: 132, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, and SEQ ID NO: 141.
- 45. An isolated *H. pylori* secreted polypeptide or a fragment thereof, wherein said polypeptide is encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 32, SEQ ID NO: 51, SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 22, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 53, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, and SEQ ID NO: 68.
  - 46. A fusion protein comprising an *H. pylori* polypeptide which comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146 operatively linked to a non-*H. pylori* polypeptide.

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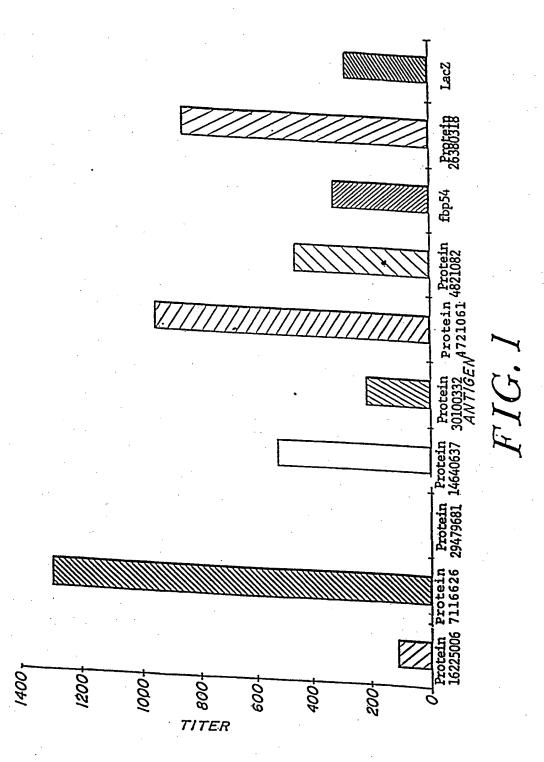
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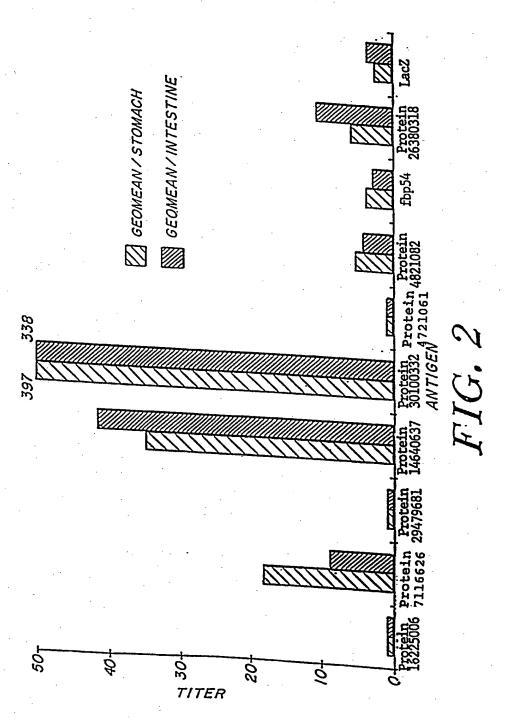
- 47. A vaccine formulation for prophylaxis or treatment of an *H. pylori* infection comprising an effective amount of at least one isolated nucleic acid of any of claims 1, 2, 3, 4, 5, 6, 7, 12, 17, 18, 19, or 20.
- 5 48. A vaccine formulation for prophylaxis or treatment of an *H. pylori* infection comprising an effective amount of at least one *H. pylori* polypeptide or a fragment thereof of any of claims 26, 27, 28, 29, 30, 31, 32, 37, 42, 43, 44 or 45.
- 49. A vaccine formulation of claim 47, further comprising a pharmaceutically acceptable carrier.
  - 50. A vaccine formulation of claim 48, further comprising a pharmaceutically acceptable carrier.
- 15 51. A vaccine formulation of claim 49, wherein the pharmaceutically acceptable carrier comprises an adjuvant.
  - 52. A vaccine formulation of claim 50, wherein the pharmaceutically acceptable carrier comprises an adjuvant.

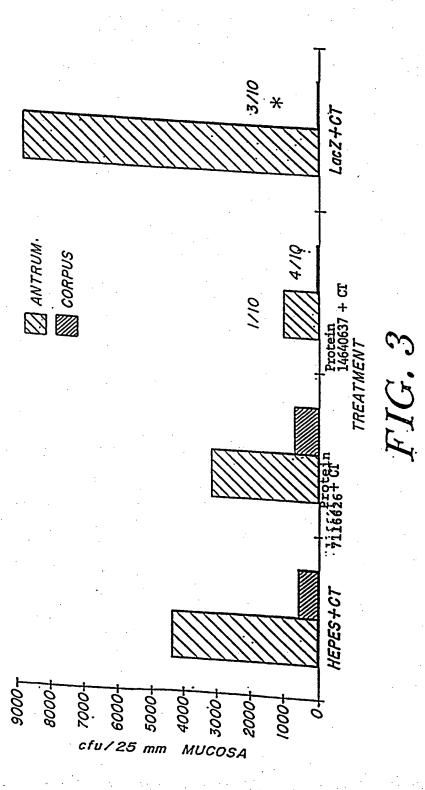
53. A vaccine formulation of claim 49, wherein the pharmaceutically acceptable carrier comprises a delivery system.

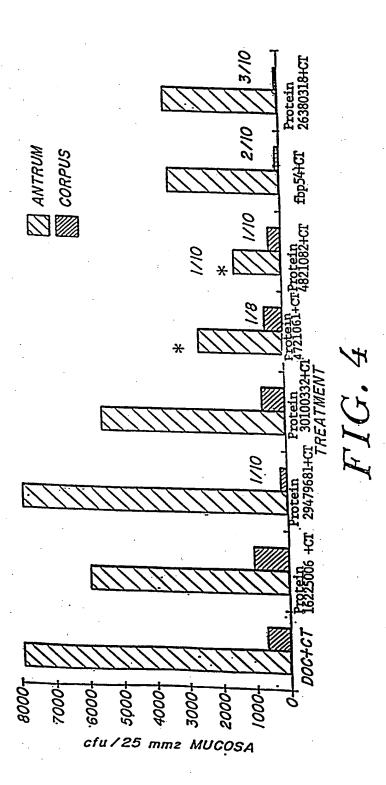
- 54. A vaccine formulation of claim 50, wherein the pharmaceutically acceptable carrier comprises a delivery system.
  - 55. A vaccine formulation of claim 53, wherein the delivery system comprises a live vector.
- 30 56. A vaccine formulation of claim 54, wherein the delivery system comprises a live vector.
  - 57. A vaccine formulation of claim 55, wherein the live vector is a bacteria or a virus.
  - 58. A vaccine formulation of claim 56, wherein the live vector is a bacteria or a virus.

- 59. A vaccine formulation of claim 53, wherein the pharmaceutically acceptable carrier further comprises an adjuvant.
- 5 60. A vaccine formulation of claim 54, wherein the pharmaceutically acceptable carrier further comprises an adjuvant.
- 61. A method of treating or reducing a risk of *H. pylori* infection in a subject comprising administering to a subject a vaccine formulation of claim 47, such that treatment or reduction of risk of *H. pylori* infection occurs.
  - 62. A method of treating or reducing a risk of *H. pylori* infection in a subject comprising administering to a subject a vaccine formulation of claim 48, such that treatment or reduction of risk of *H. pylori* infection occurs.
  - 63. A method of producing a vaccine formulation comprising: combining at least one isolated *H. pylori* polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146 with a pharmaceutically acceptable carrier to thereby form a vaccine formulation.
    - 64. A method of producing a vaccine formulation comprising:
  - (a) providing at least one isolated *H. pylori* polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146; and
- (b) combining at least one said isolated *H. pylori* polypeptide or a fragment thereof with a pharmaceutically acceptable carrier to thereby form a vaccine formulation.
  - 65. A method of producing a vaccine formulation comprising:
- (a) culturing a cell under condition that permit expression of an H.
   30 pylori polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146;
  - (b) isolating said H. pylori polypetide from said cell; and
- (c) combining at least one said isolated *H. pylori* polypeptide or a fragment thereof with a pharmaceutically acceptable carrier to thereby form a vaccine
   formulation.









aa Sed	IID#
74	BLOCK A  BLOCK A  BLOCK A  BLOCK A  BLOCK A
115	MIKRIAC-ILSLSASLALAGEVNGFFMGAGYQQGRYGPYNSNY
87	MKKFFSQSLLAL-IISMNAVSGMDGNGVFLGAGYLQGDAQMHADIN
116	MKKFFSQSLLAL-IISMNAVSGMDGNGVFLGAGYLQGDAQMHADIN
84	marulmkkfvalgllsavlsssllaegigvyigtnyqlgparlnsniyntgdctgs
•	# # # # # # # # # # # # # # # # # # #
	* * . *
	Dr oon -
74	BLOCK B BLOCK C  BLOCK B  BLOCK C  KWFGARV
115	KWFGARV
87	SDWRHGN-DLYGLNFKLGFVGFANKWFGARV
116	
84	VVGCPPGLTANKHNPGGTNINWHSKYANGALLGFGLNVGYKKF-QFKSLDMTSKWFGFRV
	· · · · · · · · · · · · · · · · · · ·
74	YGFLDWFNTSGTEHT
115	YGFLUWFNTSGTEHTKTNLLTYGGGGD YGFLUWFNTSGTEHTKTNLLTYGGGGD
87	YGFFLYAHANSIKLKNPNYNSEAAQVASQILGKQEINRLTNIADPRTFEPNMLTYGGAMD
116	YGFFIYAHANSIKLKNPNYNSEAAQVASQILGKQEINRLTNIADPRTFEPNMLTYGGAMD YGLFTYGHADLGKONY
84	YGLFLYGHADLGKQVYAPNKIQLDMVSWGVGSD
	** *
	BLOCK D
74	LIVNLIPLDKFALGLIGGVOLAGNTWMFDVDVDO
115	LIVNLIPLDKFALGLIGGVOLAGNTWMFPVDVNO
87	VIIVIVATINGTINGLIGATIGGTOLAGNSWI.MAMDCERCTTIRGAT
116	****** THE THIS LIGHT GG LOLAGNSWI, MATTICE TO THE CARE
84	LLADIIDKDNASFGIFGGVAIGGNTWKSSAANYWKEQIIEAKGPDVCTPTYCNPNAPYST
	* **. **.
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	BLOCK E BLOCK F
7.4	THE QUELWINLEGEMENT CONTROL OF THE PROPERTY OF
115	
87	THE PERSON OF TH
116	THE TAX OF THE PROPERTY OF THE
84	NTSTVAFQVWLNFGVRANIYKHNGVEFGVRVPLLINKFLSAGPNATNLYYHLKRDYSLYL
	** * * * * **
74	
74	DYVFTF
115 87	DYVFTF
	NYVFTF
116	NYVFTF
84	GYNYTF
	* **
	•

aaSeqID#	
83	MRKLFIPLLLFSALEANEKNGFFIEAGFETGLLEGTQTQEKRHTTTKNTYATYNYLPTDT
89	
108	MRKLFJPLLLFSALEANEKNGFFIEAGFETGLLEGTQTQEKRHTTTKNTYATYNYLPTDT
118	MRKLFIPLLLFSALEANEKNGFFIEAGPETGLLEGTQTQEKRHTTTKNTYATYNYLPTDT
•	
83	ILKRAANLFTNAEAISKLKFSSLSPVRVLYMYNGQLTIENFLPYNLNNVKLSFTDAQGNV
89	
108	ILKRAANLFTNAEAISKLKFSSLSPVRVLYHYNGQLTIENFLPYNLNNVKLSFTDAQGNT
118	ILKRAANLFTNAEAISKLKFSSLSPVRVLYMYNGQLTIENFLPYNLNNVKLSFTDAQGNV
• .	*****
83	IDLGVIETIPKHSKIVLPGEAFDSLKIDPYTLFLPKIEATSTSISDANTORVFET
89	VIETIPKHSKIVLPGEAFDSLKEAFDKIDPYTFFFPKFEATSTSISDINTQRVFET
108	IDLGVIETIPKHSKIVLPGEAFDSLKEAFDKIDPYTLPLPKFEATSTSISDINTQRVFET
118	IDLGVIETIPKHSKIVLPGEAFDSLKIDPYTLFLPKIEATSTSISDANTQRVFET
	**************************************
83	LNKIKTNLVVNYRNENKFKDHENHWEAFTPQTAEEFTNLMLNMIAVLDS
89	LNNIKTNLIMKYSNENPNNFNTCPYNNNGNTKNDCWQNFTPQTAEEFTNLMLNMIAVLDS
108	LNNIKTNLIMKYSNENPNNFNTCPYNNNGNTKNDCWQNFTPQTAEEFTNLMLNMIAVLDS
118	LNKIKTNLVVNYRNENKFKDHENHWEAFTPQTAEEFTNLMLNMIAVLDS
	** ***** * * * * * * * * * * * * * * * *
83	QSWGDAILNAPFEFTNSPTDCDNDPSKCVNPGTNGLVNSKVDQKYVLNKQDIVNKFKNKA
89	QSWGDAILNAPFEFTNSSTDCDSDPSKCVNPGVNGRVDTKVDQQYILNKQGIINNFRKKI
108	QSWGDAILNAPFEFTNSSTDCDSDPSKCVNPGVNGRVDTKVDQQYILNKQGIINNFRKKI
118	QSWGDAILNAPFEFTNSPTDCDNDPSKCVNPGTNGLVNSKVDOKYVLNKQDIVNKFKNKA
	*************
83	DLDVIVLKDSGVVGLGSDITPSNNDDGKHYGQLGVVASALDPKKLFGDNLKTINLEDLRT
89	EIDAVVLKNSGVVGLANGYGNDG-EYGTLGVEAYALDPKKLFGNDLKTINLEDLRT
108	EIDAVVLKNSGVVGLANGYGNDG-EYGTLGVEAYALDPKKLFGNDLKTINLEDLRT
118	DLDVIVLKDSGVVGLGSDITPSNNDDGKHYGQLGVVASALDPKKLFGDNLKTINLEDLRT
	** *** ***** ** ** ** ** * * ******* ****
83	ILHEFSHTKGYGHNGNMTYQRVPVTKDGQVEKDSNGKPKDSDGLPYNVC
89	ILHEF SHTKGYGHNGNMTYQRVPVTKDGQVEKDSNGKPKDSDGLPYNVCSLYGGSNQPAF
108	ILHEFSHTKGYGHNGNMTYQRVPVTKDGQVEKDSNGKPKDSDGLPYNVCSLYGGSNQPAF
118	ILHEFSHTKCYGHNGNMTYQRVPVTKDGQVEKDSNGKPKDSDGLPYNVCSLYGGSNQPAF
220	**************************************
83	
89	PSNYPNSIYHNCADVPAGFLGVTAAVWQQLINQNALPINYANLGSQTNYNLNASLNTODL
108	PSNYPNSIYHNCADVPAGFLGVTAAVWQQLINQNALPINYANLGSQTNYNLNASLNTQDL
118	PSNYPNSIYHNCADVPAGFLGVTAAVWQQLINQNALPINYANLGSQTNYNLNASLNTQDL
	***********

FIGURE 6 (Cont'd)

•		
89	ANSMLSTIQKTFVTSSVTNHHFSNASOSFRSPILGVNAKIGYONYFNDFIGLAYYGIIKY	
108	ANSMLSTIOKTFVTSSVTNHHFSNASOSFRSPILGVNAKIGYONYFNDFIGLAYYGIIKY	
118	ANSMLSTIQKTFVTSSVTWHFSNASQSFRSPILGVNAKIGYQNYFNDFIGLAYYGIIKY	
	· · · · · · · · · · · · · · · · · · ·	
83		
89	NYAKAVNQKVQQLSYGGGIDLLLDFITTYSNKNSPTGIQTKRNF5SSFGIFGGLRGLYNS	
108	NYAKAVNQKVQQLSYGGGIDLLLDFITTXSNKNSPTGIQTKRNFSSSFGIFGGLRGLYNS	
118	NYAKAVNQKVQQLSYGGGIDLLLDFITTXSNKNSPTGIQTKRNFSSSFGIFGGLRGLYNS	
	· · · · · · · · · · · · · · · · · · ·	
83		
89	YYVLNKVKGSGNLDVATGLNYRYKHSKYSVGISIPLIORKASVVSSGGDYTNSFVFNEGA	
108	YYVLMKVKGSGNLDVATGLNYRYKHSKYSVGISIPLIORKASVVSSGGDYTNSFVFNEGA	
118	YYVLNKVKGSGNLDVATGLNYRYKHSKYSVGISIPLIQRKASVVSSGGDYTNSFVFNEGA	*
83		
83	SHFKVFFNYGGCF	
108	SHEKVFENYGWVF	
118	Shekvfenygwve	

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aaSeqID 80	WI KEOKI DI LEVETI VIVOGDI I STORING
112	VLKFQKLPLLFVSILYNQSPLLAFDYKFSGVAESVSKVGFNHSKLNSKEGIFPTATFVTA
112	VSYDNTDDYYFPRNGVIFSSYATMSGLPSSGTLNSW
	* * * * * * * * * * * * * * * * * * * *
	BLOCK B
80	TIKLQVDSNLLPKNIEKHSLKIGVGGILGALAYDSTKTLIDQATHQIYGSELFYLIGRWW
112	NGLGGNVRNTKVYGKFAYHHLQKYLLIDLIARFK
	* **
80	CPI CNI DUIVDGI TRODI UMBILLIO
112	GFLGNAPWKDSLIESDAHTRNYVLYNSYLFYSYGDKFHLKLGRYLSNMDFMSSYTQGFEL
112	TQGGYIFRYNTDDYLPLNSTFYMGGVTTVRGFRNG
	* * * * * * * * * * * * * * * * * * * *
	BLOCK C
80	DYKINSKIALKWFSSFGRALAFGQWIRDWYAPIVTEDGRKEVYDGIHAAQLYFSSKHVQV
112	GDGIFTASTELS
	* ** *
	•
80	MPFAYFSPKIYGAPGVKIHIDSNPKFKGLGLRAQTTINVIFPVYAKDLYDVYWRNSKIGE
112	YGWI VA AVIOLA SUPPRISON MENUNCHI VI WKNSKIGE
	YGVLKAAKMRLAWFFDFGFLTFKTPTRGSFFYN
	" , *
80	BLOCK D
112	WGASLLIHQREDYNEFNFGFGYYQNFGNANARIGWYGNPIPFNYRNNSVYGGVFSNAITA
112	APTTTANFIDYGVVGAGFERATWRASTGLQIEWISPMGPLVL
	· · · · · · · · · · · · · · · · · · ·
80	DAVSGYVFGGGVYRGFLWGILGRYTYATRASERSINLNLGYKWGSFARVDVNLEYYVVSM
112	IFPIAFFN
	* **
	BLOCK E
80	HNGYRLDYLTGPFNKAFKADAQDRSNLMVSMKFFF
112	GNGKKCKGLCFNPNMNDYTQHFEFSMGTRF
	**
	<u> </u>

FIGURE 7

81  MKTNGHEKUF-AWKKCFLGASVLIGCAMNPSAETKKPNDAKNQOPVQTHERMTTSSE  82  HVTPLDFNYPUHIVQAPQNHHVGILMPRIQVSDN-LKPYIDKFQDALINQIQTIFEKRG  83  KVQALDEKILLIRPAFQXSDNIAKEYENKFKNQTTLKVEEILQNQG  KVQALDEKILLIRPAFQXSDNIAKEYENKFKNQTTLKVEEILQNQG  KVQALDEK
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FIGURE 8

## INTERNATIONAL SEARCH REPORT

International application No. PCT/US97/19575

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IPC(6)	SSIFICATION OF SUBJECT MATTER :A01N 43/04; A61K 31/70; C12Q 1/68	* . •	
	:514/44; 435/6 o International Patent Classification (IPC) or to both	national classification and IPC	
	DS SEARCHED		
	ocumentation searched (classification system follows	ed by classification symbols)	
		ed by classification symbols,	
U.S. :	514/44; 435/6		
Documental	tion searched other than minimum documentation to th	e extent that such documents are included	in the fields searched
GENEBA			
	·	·	
Electronic o	data base consulted during the international search (r	name of data base and, where practicable	, search terms used)
NONE			
C. DOC	UMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where a	appropriate, of the relevant passages	Relevant to claim No.
Α	TAYLOR, et al. Construction of a Hel	licobacter pylori Genome Map	1-65
	and Demonstration of Diversity at th	1	
	Bacteriology. November 1992, Vol. 1		
	see entire document.	, , ,	
A	AKOPYANZ, et al. DNA diversity	y among clinical isolates of	1-65
	Helicobacter pylori detected by PCR	-based RAPD fingerprinting.	·
	Nucleic Acids Research. 1992, Vol. 2	<del>-</del> - 1	
	see entire document.		
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Furth	er documents are listed in the continuation of Box (	C. See patent family annex.	•
• Sp	ecial categories of cited documents:	"T" later document published after the inte	
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E" car	her document published on or after the international filing date	"X" document of particular relevance, the considered novel or cannot be considered.	
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•O• doc	cument referring to an oral disclosure, use, exhibition or other	combined with one or more other such being obvious to a person skilled in th	documents, such combination
'P' doc	nument published prior to the international filing date but later than priority date claimed	*&* document member of the same patent	1
Date of the	actual completion of the international search	Date of mailing of the international sea	rch report
27 FEBRU	JARY 1998	1 3 MAR 1998	
Name and m	nailing address of the ISA/US	Authorized officer	$\bigcirc$
Commissioner of Patents and Trademarks			
Box PCT Washington, D.C. 20231		GINNY PORTNER /! W/	
Facsimile N	o. (703) 305-3230	Telephone No. (703) 308-0196	4/

# INTERNATIONAL SEARCH REPORT

International application No. PCT/US97/19575

Box 1 Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
Please See Extra Sheet.
As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all scarchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. X As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
1-65, SEQ. ID Nos. 1, 7, 8, 11, 37, 39, 43, 45, 55, 61, 74, 80, 81 and 112
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest.
X No protest accompanied the payment of additional search fees.

### INTERNATIONAL SEARCH REPORT

International application No. PCT/US97/19575

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-26, 47, 49, 51, 53, 55, 57, 59, and 61, drawn to no fewer than 135 nucleic acid molecules, vectors containing the nucleic acid molecules, DNA encoding fragments of the polypeptides encoded by the no fewer than 135 different DNAs, organism transformed with the nucleic acid molecules, vaccines and methods of producing polypeptides encoded by the no fewer than 135 different nucleic acid molecules.

Group II, claim(s) 27-46, 48, 50, 52, 54, 56, 58, 60, and 62-65 are, drawn to no fewer than 73 polypeptides encoded by a subset of the encoding DNA mentioned in Group I.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

Group I contains a separate DNA species for each sequence mentioned. Therefore, there is a minimum of 135 species.

Group II contains at least one polypeptide for each DNA sequence mentioned. Therefore, this is a minimum of 73 species in Group II.

For either Group that applicant elects, a total of 10 (ten) specified sequences will be searched and no more than 4 (four) specified sequences will be searched for each additional fee paid; if no additional fee is paid and no election indicated the first 10 sequences appearing in Group I will be searched.

and it considers that the International Application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups I and II do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The polypeptide encoding DNAs, vectors containing them, organisms transformed with them and methods of polypeptide production using them of Group I are materially different from each other and are therefore independent from the polypeptides of Group II. Additionally, none of the products or methods of Group I is needed to make the polypeptides of Group II.

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: There is no relationship between or among the various nucleotide and amino acid sequences mentioned in the claims.

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